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PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

To:

Commissioner
US Department of Commerce
United States Patent and Trademark Office, PCT
2011 South Clark Place Room CP2/5C24
Arlington, VA 22202
ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 15 January 2001 (15.01.01)	
International application No. PCT/EP00/03306	**Applicant's or agent's file reference** 7362 PCT
International filing date (day/month/year) 13 April 2000 (13.04.00)	**Priority date** (day/month/year) 27 April 1999 (27.04.99)
Applicant SCHMIDT, Stefan	

1. The designated Office is hereby notified of its election made:

   [X] in the demand filed with the International Preliminary Examining Authority on:

   24 November 2000 (24.11.00)

   [ ] in a notice effecting later election filed with the International Bureau on:

2. The election [X] was

   [ ] was not

   made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO **34, chemin des Colombettes** **1211 Geneva 20, Switzerland**	Authorized officer Yolaine CUSSAC
Facsimile No.: (41-22) 740.14.35	Telephone No.: (41-22) 338.83.38

VERTRAG ÜBER [redacted] INTERNATIONALE ZUSAM[redacted]NARBEIT AUF DEM GEBIET DES PATENTWESENS

PCT

INTERNATIONALER VORLÄUFIGER PRÜFUNGSBERICHT

(Artikel 36 und Regel 70 PCT) T 4

Aktenzeichen des Anmelders oder Anwalts	WEITERES VORGEHEN	siehe Mitteilung über die Übersendung des internationalen vorläufigen Prüfungsberichts (Formblatt PCT/IPEA/416)
7362 PCT		
Internationales Aktenzeichen	Internationales Anmeldedatum *(Tag/Monat/Jahr)*	Prioritätsdatum *(Tag/Monat/Tag)*
PCT/EP00/03306	13/04/2000	27/04/1999
Internationale Patentklassifikation (IPK) oder nationale Klassifikation und IPK G01N21/25		
Anmelder CARL ZEISS JENA GMBH et al.		

1. Dieser internationale vorläufige Prüfungsbericht wurde von der mit der internationalen vorläufigen Prüfung beauftragten Behörde erstellt und wird dem Anmelder gemäß Artikel 36 übermittelt.

2. Dieser BERICHT umfaßt insgesamt 6 Blätter einschließlich dieses Deckblatts.

   ☒ Außerdem liegen dem Bericht ANLAGEN bei; dabei handelt es sich um Blätter mit Beschreibungen, Ansprüchen und/oder Zeichnungen, die geändert wurden und diesem Bericht zugrunde liegen, und/oder Blätter mit vor dieser Behörde vorgenommenen Berichtigungen (siehe Regel 70.16 und Abschnitt 607 der Verwaltungsrichtlinien zum PCT).

   Diese Anlagen umfassen insgesamt 2 Blätter.

3. Dieser Bericht enthält Angaben zu folgenden Punkten:

   - I ☒ Grundlage des Berichts
   - II ☐ Priorität
   - III ☐ Keine Erstellung eines Gutachtens über Neuheit, erfinderische Tätigkeit und gewerbliche Anwendbarkeit
   - IV ☐ Mangelnde Einheitlichkeit der Erfindung
   - V ☒ Begründete Feststellung nach Artikel 35(2) hinsichtlich der Neuheit, der erfinderischen Tätigkeit und der gewerblichen Anwendbarkeit; Unterlagen und Erklärungen zur Stützung dieser Feststellung
   - VI ☐ Bestimmte angeführte Unterlagen
   - VII ☐ Bestimmte Mängel der internationalen Anmeldung
   - VIII ☐ Bestimmte Bemerkungen zur internationalen Anmeldung

Datum der Einreichung des Antrags	Datum der Fertigstellung dieses Berichts
24/11/2000	16. 07. 01
Name und Postanschrift der mit der internationalen vorläufigen Prüfung beauftragten Behörde: Europäisches Patentamt D-80298 München Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Bevollmächtigter Bediensteter Mason, W Tel. Nr. +49 89 2399 2623

INTERNATIONALER VORLÄUFIGER PRÜFUNGSBERICHT

Internationales Aktenzeichen PCT/EP00/03306

I. Grundlag d s Berichts

1. Hinsichtlich der **Bestandteile** der internationalen Anmeldung (*Ersatzblätter, die dem Anmeldeamt auf eine Aufforderung nach Artikel 14 hin vorgelegt wurden, gelten im Rahmen dieses Berichts als "ursprünglich eingereicht" und sind ihm nicht beigefügt, weil sie keine Änderungen enthalten (Regeln 70.16 und 70.17)*): , **Beschreibung, Seiten:**

1-4	ursprüngliche Fassung

Patentansprüche, Nr.:

1-13	eingegangen am	23/05/2001	mit Schreiben vom	23/05/2001

Zeichnungen, Blätter:

1/4-4/4	ursprüngliche Fassung

2. Hinsichtlich der **Sprache**: Alle vorstehend genannten Bestandteile standen der Behörde in der Sprache, in der die internationale Anmeldung eingereicht worden ist, zur Verfügung oder wurden in dieser eingereicht, sofern unter diesem Punkt nichts anderes angegeben ist.

   Die Bestandteile standen der Behörde in der Sprache: zur Verfügung bzw. wurden in dieser Sprache eingereicht; dabei handelt es sich um

   - ☐ die Sprache der Übersetzung, die für die Zwecke der internationalen Recherche eingereicht worden ist (nach Regel 23.1(b)).
   - ☐ die Veröffentlichungssprache der internationalen Anmeldung (nach Regel 48.3(b)).
   - ☐ die Sprache der Übersetzung, die für die Zwecke der internationalen vorläufigen Prüfung eingereicht worden ist (nach Regel 55.2 und/oder 55.3).

3. Hinsichtlich der in der internationalen Anmeldung offenbarten **Nucleotid- und/oder Aminosäuresequ nz** ist die internationale vorläufige Prüfung auf der Grundlage des Sequenzprotokolls durchgeführt worden, das:

   - ☐ in der internationalen Anmeldung in schriftlicher Form enthalten ist.
   - ☐ zusammen mit der internationalen Anmeldung in computerlesbarer Form eingereicht worden ist.
   - ☐ bei der Behörde nachträglich in schriftlicher Form eingereicht worden ist.
   - ☐ bei der Behörde nachträglich in computerlesbarer Form eingereicht worden ist.
   - ☐ Die Erklärung, daß das nachträglich eingereichte schriftliche Sequenzprotokoll nicht über den Offenbarungsgehalt der internationalen Anmeldung im Anmeldezeitpunkt hinausgeht, wurde vorgelegt.
   - ☐ Die Erklärung, daß die in computerlesbarer Form erfassten Informationen dem schriftlichen Sequenzprotokoll entsprechen, wurde vorgelegt.

4. Aufgrund der Änderungen sind folgende Unterlagen fortgefallen:

- ☐ Beschreibung, Seiten:
- ☐ Ansprüche, Nr.:
- ☐ Zeichnungen, Blatt:

5. ☐ Dieser Bericht ist ohne Berücksichtigung (von einigen) der Änderungen erstellt worden, da diese aus den angegebenen Gründen nach Auffassung der Behörde über den Offenbarungsgehalt in der ursprünglich eingereichten Fassung hinausgehen (Regel 70.2(c)).

   (Auf Ersatzblätter, die solche Änderungen enthalten, ist unter Punkt 1 hinzuweisen;sie sind diesem Bericht beizufügen).

6. Etwaige zusätzliche Bemerkungen:

V. Begründete Feststellung nach Artikel 35(2) hinsichtlich der Neuheit, der erfinderischen Tätigkeit und der gewerblichen Anwendbarkeit; Unterlagen und Erklärungen zur Stützung dieser Feststellung

1. Feststellung

Neuheit (N)	Ja:	Ansprüche	1-13
	Nein:	Ansprüche	
Erfinderische Tätigkeit (ET)	Ja:	Ansprüche	
	Nein:	Ansprüche	1-13
Gewerbliche Anwendbarkeit (GA)	Ja:	Ansprüche	1-13
	Nein:	Ansprüche	

2. Unterlagen und Erklärungen
   siehe Beiblatt

ZU PUNKT V

1. Die vorliegende Anmeldung betrifft eine Anordnung zur optischen Auswertung eines Gegenstandsarrays (z.B. einer Mikrotiterplatte), wobei alle Pupillen eines dem Gegenstandsarray vorgeordneten Minilinsenarrays durch eine Feldlinse gleichzeitig auf ein Detektorarray abgebildet werden - eine Beleuchtung wird zwischen der Feldlinse und einem Objektiv eingekoppelt.

   Die folgenden Dokumente werden genannt:

   D2= "Parallel, confocal, and complete spectrum imager for fluorescent detection of high-density microarray"; Bogdanov Valery ; Boyce-Jacino Michael; Proceedings of the 1999 Three-Dimensional and Multidimensional Microscopy: Image Acquisition and Processing VI; San Jose, CA, USA; Jan 24-Jan 25 1999.
   D3=US4892409; D4=DE19725050

2. Was den Wortlaut des Anspruchs 1 betrifft wird auf die folgenden Punkte hingewiesen:

   a) Die Beleuchtung stellt kein physikalisches Merkmal der Anordnung dar.

   b) Das Gegenstandsarray stellt kein Merkmal der Anordnung zur optischen Auswertung dar.

3. NEUHEIT

   D2 (Fig. 1; S. 298-300) stellt den nächstliegenden Stand der Technik dar und offenbart alle Merkmale der unabhängigen Ansprüche 1, 12, 13 außer:

   i) der Anordnung des Strahlenteilers zwischen der Feldlinse und dem Objektiv.

   Ansprüche 1-13 erfüllen daher das Erfordernis der Neuheit (Art. 33. 2 PCT).

4. ERFINDERISCHE TÄTIGKEIT

4.1 Unabhängiger Anspruch 1

Zu i):
Dieses Merkmal entspricht einer üblichen Abänderung der geometrischen optischen Anordnung in D2, wobei die obere Beleuchtungsanordnung (d.h. Laserquelle, Strahlteiler, Strahlaufweiter) nach unten zwischen die Linsen L1, L2 plaziert wird, so daß beide Strahlteiler auf der gleichen horizontalen Ebene liegen. Diese Umstellung bedarf keiner zusätzlichen Komponenten, hat keine Nachteile was die Genauigkeit der Messungen betrifft, und stellt eine gleichwertige alternative optische Anordnung dar - sie wäre daher dem Fachmann naheliegend.

Der Anspruch 1 erfüllt daher nicht das Erfordernis der erfinderischen Tätigkeit (Art. 33.3 PCT).

4.2 Abhängige Ansprüche 2-13

Die zusätzlichen Merkmale der folgenden Ansprüche gehen, aus den angegebenen Gründen, auch in naheliegender Weise, aus dem Stand der Technik hervor:

Ansprüche 2-5. Sind in der optischen Anordnung gemäß D2, Fig. 1 offenbart bzw. folgen zwangsläufig nach deren obigen Umstellung.

Anspruch 6. Das Gegenstandsarray ist vertikal verschiebbar. Zur richtigen Positionierung (d.h. Fokussierung) der Probe (des Gegendstandsarrays) bezüglich der optischen Anordnung ist es üblich, auf dem Gebiet des Dokuments D2, diese auf einem Schiebetisch zu montieren, der entlang der optischen Achse linear bewegbar ist.

Ansprüche 7-8, 10, 12. D2 beschäftigt sich D2 mit der Abbildung von Mikroarrays durch Fluoreszenz und spricht auf S. 306 direkt die zeitaufgelöste Fluoreszenzmessung an.

Anspruch 9. Die Option, daß das Minilinsenarray "austauschbar" ist, ist zwangsläufig bei jedem Minilinsenarray vorhanden.

Anspruch 11. Die Absorptionsmessung ist als naheliegende Alternative zur Fluoreszenzmessung aus D3, D4 bekannt.

Anspruch 13. Dieser Anspruch bezieht sich auf die Verwendung der Anordnung als Reader für Mikrotiterplatten. D2 offenbart eine Auswertung von Probenarrays in Form von Punktproben auf einem Substrat. D3 (Fig. 4b) liegt auf dem gleichen Gebiet wie D2 und offenbart als Probe eine Mikrotiterplatte.

Ansprüche 2-13 erfüllen daher nicht das Erfordernis der erfinderischen Tätigkeit (Art. 33.3 PCT) angesichts der Dokumente D2, D3/D4.

Anmelderin: Carl Zeiss Jena GmbH
(Anwaltsakte: Pat 1250/107-01-PCT)
Amtsaktenzeichen: PCT/EP 00/03306

K/22/ao(bst)
23. Mai 2001.

Geänderte Patentansprüche

1. Anordnung zur optischen Auswertung eines Gegenstandsarrays (1), mit
- einem Detektorarray (7),
- einem dem Gegenstandsarray (1) in Richtung des Detektorarrays (7) vorgeordneten Minilinsenarray (2),
- einer dem Gegenstandsarray (1) in Richtung des Detektorarrays (7) vorgeordneten Feldlinse (3),
- einer Lichtquelle (15), deren Strahlung über einen Strahlteiler (8) zwischen der Feldlinse (3) und einem Objektiv (6) eingekoppelt ist,
- wobei das Objektiv (6) zusammen mit der Feldlinse (3) alle Pupillen des Minilinsenarrays (2) gleichzeitig auf das Detektorarray (7) abbildet.

2. Anordnung nach Anspruch 1, bei der die Feldlinse (3) und eine weitere Linse (11) eine teleskopische Anordnung bilden, die das Gegenstandsarray (1) mit Licht der Lichtquelle (15) beleuchtet.

3. Anordnung nach einem der obigen Ansprüche, mit einer zwischen Feldlinse (3) und Objektiv (6) angeordneten Blende (4a), wobei der Strahlteiler (8) zwischen der Blende (4a) und der Feldlinse (3) liegt.

4. Anordnung nach einem der obigen Ansprüche, bei der die Feldlinse (3) und das Objektiv (6) eine telezentrische Abbildung der Pupillenebene des Minilinsenarrays (2) auf das Detektorarrays (7) bewirken.

5. Anordnung nach einem der obigen Ansprüche, bei der zwischen der Feldlinse (3) und der Blende (4a) ein oder mehrere Umlenkelemente (17, 18) zur Faltung des Strahlenganges für Beleuchtung und/oder Detektion vorgesehen sind.

6. Anordnung nach einem der obigen Ansprüche, bei der das Gegenstandsarray (1) mindestens vertikal zur Beleuchtungsachse verschiebbar ist.

7. Anordnung nach einem der obigen Ansprüche, bei der zur zeitaufgelösten Fluoreszenzmessung die Lichtquelle (15) intermittierend schaltbar und eine zum Beleuchtungstakt synchronisierte, vorzugsweise dazu zeitversetzte Detektion möglich ist.

8. Anordnung nach Anspruch 7, mit einer Blitzlampe als Lichtquelle (15).

9. Anordnung nach einem der obigen Ansprüche, bei der das Minilinsenarray (2) zur Beobachtung des vollständigen Gegenstandsarrays (1) aus dem Strahlengang ausschwenkbar und/oder zur Anpassung an unterschiedliche Meßausgaben austauschbar ist.

10. Anordnung nach einem der obigen Ansprüche, bei der die Lichtquelle (15) zur Luminiszenzdetektion ausschaltbar und/oder ein die Strahlung der Lichtquelle (15) einkoppelndes Einkoppelelement (8) ausschwenkbar ist.

11. Anordnung nach einem der obigen Ansprüche, bei der für eine Absorptionsmessung dem Gegenstandsarray (1) in Beleuchtungsrichtung ein zweites Detektorarray nachgeordnet ist.

12. Verwendung einer Anordnung nach einem der obigen Ansprüche in einem Kombinationsgerät zur Messung mindestens eines der folgenden Effekte am Gegenstandsarray (1): Fluoreszenz, zeitaufgelöste Fluoreszenz, Lumineszenz und Absorption.

13. Verwendung einer Anordnung nach einem der Ansprüche 1 bis 11 als Reader für Mikrotiterplatten.

Translation

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

3

Applicant's or agent's file reference 7362 PCT	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/EP00/03306	International filing date (*day/month/year*) 13 April 2000 (13.04.00)	Priority date (*day/month/year*) 27 April 1999 (27.04.99)
International Patent Classification (IPC) or national classification and IPC G01N 21/25		
Applicant CARL ZEISS JENA GMBH		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 6 sheets, including this cover sheet.

   ☒ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 2 sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
24 November 2000 (24.11.00)	16 July 2001 (16.07.2001)
Name and mailing address of the IPEA/EP Facsimile No.	Authorized officer Telephone No.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/EP00/03306

I. Basis of the report

1. This report has been drawn on the basis of (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments.*):

☐ the international application as originally filed.

☒ the description, pages 1-4, as originally filed,
pages _____, filed with the demand,
pages _____, filed with the letter of _____,
pages _____, filed with the letter of _____.

☒ the claims, Nos. _____, as originally filed,
Nos. _____, as amended under Article 19,
Nos. _____, filed with the demand,
Nos. 1-13, filed with the letter of 23 May 2001 (23.05.2001),
Nos. _____, filed with the letter of _____.

☒ the drawings, sheets/fig 1/4-4/4, as originally filed,
sheets/fig _____, filed with the demand,
sheets/fig _____, filed with the letter of _____,
sheets/fig _____, filed with the letter of _____.

2. The amendments have resulted in the cancellation of:

☐ the description, pages _____
☐ the claims, Nos. _____
☐ the drawings, sheets/fig _____

3. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

4. Additional observations, if necessary:

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	1-13	YES
	Claims		NO
Inventive step (IS)	Claims		YES
	Claims	1-13	NO
Industrial applicability (IA)	Claims	1-13	YES
	Claims		NO

2. Citations and explanations

1. The present application relates to a device for the optical evaluation of an object array (e.g. a microtitre plate), wherein all of the pupils of a minilens array arranged in front of the object array are simultaneously displayed by a field lens on a detector array - an illuminating device is coupled between the field lens and an objective.

The following documents are cited:

D2: "Parallel, confocal, and complete spectrum imager for fluorescent detection of high-density microarray"; Bogdanov Valery; Boye-Jacino Michael; Proceedings of the 1999 Three-Dimensional and Multidimensional Microscopy: Image Acquisition and Processing VI; San Jose, CA, USA; Jan 24-Jan 25 1999

D3: US-A-4 892 409

D4: DE-A-197 25 050.

2. The following points are made with respect to the wording of Claim 1:

a) the illuminating device is not a physical feature

of the device;
b) the object array is not a feature of the device for optical evaluation.

3. NOVELTY

D2 (Fig. 1, pp. 298-300) is the closest prior art and discloses all of the features of independent Claims 1, 12 and 13, except:

i) the arrangement of the beam splitter between the field lens and the objective.

Claims 1 to 13 therefore meet the novelty requirements (PCT Article 33(2)).

4. INVENTIVE STEP

4.1 Independent Claim 1

Re. i):
This feature represents a standard alteration of the geometrical optical device in D2, wherein the upper illuminating device (i.e. laser source, beam splitter, beam expander) is placed lower down between the lenses L1 and L2, such that both beam splitters are on the same horizontal plane. This rearrangement does not require additional components, has no disadvantages with respect to the precision of the measurements, and constitutes an equivalent alternative optical device. It would therefore be obvious to a person skilled in the art.

Claim 1 does not therefore meet the inventive step requirements (PCT Article 33(3)).

4.2 Dependent Claims 2-13

The additional features of the following claims are also obvious from the prior art, for the following reasons:

Claims 2-5 are disclosed in the optical device as per D2, Fig. 1, or result necessarily from the rearrangement of same discussed above.

Claim 6: The object array can be vertically displaced. To position the sample (the object array) correctly (i.e. focussing), it is normal, in the field of document D2, to mount said device on a slide table which can be moved linearly along the optical axis.

Claims 7-8, 10, 12: D2 is concerned with the representation of microarrays using fluorescence and, on p. 306, directly addresses the measurement of fluorescence.

Claim 9: The option that the microlens array is "replaceable" necessarily holds for any microlens array.

Claim 11: The measurement of absorption is known from D3 and D4 as an obvious alternative to the measurement of fluorescence.

Claim 13: This claim relates to the use of the device as a reader for microtitre plates. D2

discloses an evaluation of sample arrays in the form of dot samples on a substrate. D3 (Fig. 4b) is in the same field as D2 and discloses, as a sample, the microtitre plate.

Claims 2-13 do not therefore meet the requirements of inventive step (PCT Article 33(3)) with respect to documents D2 and D3/D4.

Claims

1. Arrangement for optical evaluation of an object array, in front of which are disposed, in the direction of a detector array, a microlens array (MLA), preferably an exchangeable and/or rotational microlens array, and a field lens,
with an illumination being coupled by means of a beam splitter, preferably a rotational beam splitter,
wherein said illumination is coupled in between the field lens and an objective.

2. An arrangement as claimed in Claim 1,
wherein the illumination is coupled in between the field lens and a diaphragm disposed in front of the objective.

3. An arrangement as claimed in at least one of the preceding Claims, wherein a telecentric image of the pupil plane of the MLA is imaged onto the detector array.

4. An arrangement as claimed in at least one of the preceding Claims, wherein the field lens and a second lens form a telescope array for illuminating the MLA.

5. An arrangement as claimed in at least one of the preceding Claims, wherein one or more reflecting elements are provided for folding the illumination and/or detection beam path.

6. An arrangement as claimed in at least one of the preceding Claims, wherein the object array is preferably slideable, at least vertically to the axis of illumination, so as to adjust the focus.

7. An arrangement as claimed in at least one of the preceding Claims, wherein the illumination is intermittently interrupted and a detection synchronized to the illumination clock, preferably a deferred detection, is carried out so as to allow a time-dependent fluorescence measurement.

8. An arrangement as claimed in Claim 7, with illumination by a flash lamp.

9. An arrangement as claimed in at least one of the preceding Claims, wherein the MLA can be swivelled out of the beam path for observing the entire object array.

10. An arrangement as claimed in at least one of the preceding Claims, wherein the illumination can be switched off for luminescence detection and/or its coupling element can be swivelled out.

11. An arrangement as claimed in at least one of the preceding Claims, wherein a second detector array is disposed behind the object array in the illumination direction for absorption measurement.

12. An arrangement as claimed in at least one of the preceding Claims, wherein the MLA can be replaced by further MLAs so as to adapt to different measurement applications and/or different object arrays.

13. A combined device for detecting the fluorescence and/or the time-dependent fluorescence and/or the luminescence and/or the absorption of an illuminated object array using a microlens array (MLA) and a field lens as well as a detector array,
comprising an illumination, coupled in through a beam splitter,
in particular as claimed in any of the preceding Claims,
wherein the MLA and/or the detector array are exchangeable and/or rotational, and/or the beam splitter is rotational and/or a further detector array is provided for absorption measurement and/or means for focusing on the object array are provided.

14. The use of an arrangement as claimed in any of the preceding Claims as a reader for microtiter plates.

VERTRAG ÜBER DIE INTERNATIONALE ZUSAMMENARBEIT AUF DEM GEBIET DES PATENTWESENS

PCT

INTERNATIONALER RECHERCHENBERICHT

(Artikel 18 sowie Regeln 43 und 44 PCT)

Aktenzeichen des Anmelders oder Anwalts	WEITERES VORGEHEN	siehe Mitteilung über die Übermittlung des internationalen Recherchenberichts (Formblatt PCT/ISA/220) sowie, soweit zutreffend, nachstehender Punkt 5
7362 PCT		
Internationales Aktenzeichen	Internationales Anmeldedatum *(Tag/Monat/Jahr)*	(Frühestes) Prioritätsdatum *(Tag/Monat/Jahr)*
PCT/EP 00/ 03306	13/04/2000	27/04/1999
Anmelder		
CARL ZEISS JENA GMBH		

Dieser internationale Recherchenbericht wurde von der Internationalen Recherchenbehörde erstellt und wird dem Anmelder gemäß Artikel 18 übermittelt. Eine Kopie wird dem Internationalen Büro übermittelt.

Dieser internationale Recherchenbericht umfaßt insgesamt 3 Blätter.

[X] Darüber hinaus liegt ihm jeweils eine Kopie der in diesem Bericht genannten Unterlagen zum Stand der Technik bei.

1. **Grundlage des Berichts**

   a. Hinsichtlich der **Sprache** ist die internationale Recherche auf der Grundlage der internationalen Anmeldung in der Sprache durchgeführt worden, in der sie eingereicht wurde, sofern unter diesem Punkt nichts anderes angegeben ist.

   [ ] Die internationale Recherche ist auf der Grundlage einer bei der Behörde eingereichten Übersetzung der internationalen Anmeldung (Regel 23.1 b)) durchgeführt worden.

   b. Hinsichtlich der in der internationalen Anmeldung offenbarten **Nucleotid- und/oder Aminosäuresequenz** ist die internationale Recherche auf der Grundlage des Sequenzprotokolls durchgeführt worden, das

   [ ] in der internationalen Anmeldung in schriftlicher Form enthalten ist.

   [ ] zusammen mit der internationalen Anmeldung in computerlesbarer Form eingereicht worden ist.

   [ ] bei der Behörde nachträglich in schriftlicher Form eingereicht worden ist.

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C. ALS WESENTLICH ANGESEHENE UNTERLAGEN

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International Application No
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(54) Title: MICROLENS SCANNER FOR MICROLITHOGRAPHY AND WIDE-FIELD CONFOCAL MICROSCOPY

(57) Abstract

A microscopy and/or lithography system uses a comparatively low-resolution image projection system, which has a very small numerical aperture but large image field, in conjunction with a microlens array comprising miniature lens elements, each of which has a large numerical aperture but very small field. The projection system contains a small aperture stop which is imaged by the microlenses onto an array of diffraction-limited microspots on the microscope sample or printing surface at the microlens focal point positions, and the surface is scanned to build up a complete raster image from the focal point array. The system design thus circumvents the tradeoff between image resolution and field size which is the source of much of the complexity and expense of conventional wide-field, high-NA microscopy and microlithography systems. The system makes possible flat field, distortion-free imaging, with accurate overlay, focus, and warp compensation, over very large image fields (larger than the practical limits of conventional imaging means). In one embodiment it would use a Digital Micromirror Device as the image source, potentially eliminating the need for photomasks in semiconductor manufacture.

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MICROLENS SCANNER FOR MICROLITHOGRAPHY AND WIDE-FIELD CONFOCAL MICROSCOPY

CROSS-REFERENCE TO RELATED APPLICATION

This application claims priority from provisional application 60/012,434, filed Feb. 28, 1996, the disclosure of which is incorporated by reference.

BACKGROUND OF THE INVENTION

The invention relates to two fields that can be broadly categorized as "image reading" and "image writing." Its primary intended application in the image reading field would be as a tandem scanning confocal microscope, although it could also potentially be used for other applications, for example as a high-resolution document scanner, or as a reader for optical mass storage media, etc. The invention's primary intended application for image writing would be as a microlithography printer for semiconductor manufacture; however this field may also include applications such as document printing, photographic reproduction, etc. The following description will focus on the confocal microscopy and microlithography applications, although the specification can be applied by obvious extension to other applications as well.

A confocal microscope (Ref. 1) is similar to a conventional microscope except that the illumination is filtered by a small pinhole which is focused to a diffraction-limited microspot on the sample, and (in the case of a reflection confocal microscope) the light reflected from the sample is again filtered by the same pinhole. The focused beam is raster-scanned across the sample (by scanning either the pinhole or the sample) to build up a high-resolution raster image of the sample. (A transmission confocal microscope is similar, except that separate pinholes are used to filter the illumination and transmitted light.) In comparison to conventional microscopes a confocal microscope has superior lateral image resolution and also exhibits extremely fine depth resolution.

A tandem scanning confocal microscope of the Nipkow type (see Ref. 1, Chap. 14) uses an array of pinholes, rather than a single pinhole,

to achieve a very high image frame rate. The pinholes are formed on a disk which spins at a high rate to provide real-time imaging. A drawback of the Nipkow-type system is that its field size is limited by the performance of conventional microscope objectives. Given the field size limitations of commercial high-power objectives it would take a very long time for a Nipkow-type system to scan, for example, a complete semiconductor wafer, even with its high image frame rate.

In comparison to typical microscopy applications, field size requirements for microlithography steppers are far more demanding. Current steppers must achieve high-resolution, flat-field, and low-distortion imaging performance comparable to high-quality microscope objectives, but over a field size of around 20mm or greater. This level of performance is attained by using massive, multielement, all-glass projection lenses or catadioptric systems such as the Perkin-Elmer Micralign and Wynne-Dyson systems (Ref. 2, Chap. 8). The optics in such systems must be manufactured to submicron accuracies, and submicron alignment and dimensional stability tolerances must be held over large distances between massive optical and mechanical components to maintain resolution, focus and overlay accuracy. The technical difficulties associated with the combined requirements for high image resolution and large field size pose significant challenges to the further advancement of optical microlithography for semiconductor applications.

SUMMARY OF THE INVENTION

The invention provides imaging systems and techniques that circumvent the tradeoff between image resolution and field size which is the source of much of the complexity and expense of conventional wide-field, high-NA microscopy and microlithography systems.

In short, this is achieved by using a comparatively low-resolution image projection system, which has a very small numerical aperture but large image field, in conjunction with a microlens array comprising miniature lens elements, each of which has a large numerical aperture but very small field. The projection system contains a small aperture stop which is imaged by the microlenses onto an array of diffraction-limited microspots on the microscope sample or printing surface at the microlens focal point positions, and the surface is scanned to build up a complete raster image from the focal point array.

The system's critical dimensional and alignment tolerances are localized in the microlens array itself and in its positioning relative to the sample or printing surface. This minimizes the system's susceptibility to dimensional tolerance stack-up, thermal effects, and weight loading which are problematic in conventional microimaging systems. For the microlithography application, the microlens array can also function as the imaging element of a position encoder which controls the array's alignment relative to the printing surface. By making the exposure imaging optic and the position encoder optic one and the same, dimensional tolerance stack-up in the positioning servomechanism is kept to a minimum. The microlens positioning servo could accurately and precisely control *X-Y* positioning, focus, and tilt; and in one embodiment it could also compensate for warp in either the printing surface or the lens array itself.

A further understanding of the nature and advantages of the present invention may be realized by reference to the remaining portions of the specification and the drawings.

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. 1 illustrates a simple embodiment of the invention which could operate as a tandem scanning confocal microscope;

FIG. 2 illustrates a very similar embodiment which could function as a lithography printer;

FIG. 3 illustrates a variant of the lithography system which combines the printing and microscopic imaging functions in a single device;

FIGS. 4-6 illustrate several alternative scan patterns that could be used, including the bi-directional raster scan (FIG. 4), continuous line scan (FIG. 5), and segmented line scan or "multiscan" (FIG. 6);

FIG. 7 illustrates a microlens's focal plane field coordinates (X, Y) and aperture plane coordinates (X', Y');

FIG. 8 illustrates the microlens point, line, and plane exposure profiles;

FIG. 9 illustrates the exposure profile (E vs X) for an image feature and its complement;

FIG. 10 illustrates constant-exposure contours for several positive line images;

FIGS. 11a-f illustrate a multilevel processing procedure for effecting the logical operations of conjunction (logical AND) and disjunction (logical OR);

FIGS. 12 and 13 show simple illustrations of boolean compositing;

FIG. 14 illustrates the basic design tradeoffs relating to aperture sizing and microlens spacing;

FIG. 15 illustrates a possible configuration for the microlens design;

FIGS. 16a-g illustrate a fabrication process based on laser-assisted chemical etching;

FIG. 17 illustrates the exposure process for microlens replication;

FIG. 18 illustrates an alternative design configuration which simplifies the illumination optics;

FIG. 19 illustrates an even simpler illumination system;

FIG. 20 illustrates a variant of the FIG. 19 configuration in which the two collimator lenses are replaced by a single collimating mirror;

FIGS. 21a,b illustrate a configuration that is similar to FIG. 20, except that it includes a confocal viewing system which is used as a position encoder to monitor wafer alignment and focus;

FIG. 22 illustrates a design configuration which uses an object-plane microlens array in conjunction with a micromirror array;

FIG. 23 illustrates an alternative embodiment which uses a photomask in conjunction with an object-plane microlens array;

FIGS. 24 and 25 illustrate a scanned-illumination technique;

FIG. 26 illustrates the Moiré technique for X tracking;

FIG. 27 illustrates the interpolated detector signal with the Moiré technique;

FIG. 28 illustrates three interspersed microlens sets with different focus heights, h_1, h_2, and h_3;

FIG. 29 illustrates a top view (looking down on the wafer plane) of a pattern that could be used for tracking X, Y, and θ rotation;

FIG. 30 illustrates the confocal response of a 0.5NA system operating at wavelength λ = 0.633μm;

FIG. 31 illustrates two focus-sensor microlenses with their focal planes displaced respectively above and below the wafer surface by a distance ΔZ;

FIG. 32 illustrates a configuration in which the focus-sensor microlenses are designed to have a common focal plane displaced by a small distance ΔZ below the wafer surface, and portions of the wafer surface (e.g., areas within the scribe lines) are etched to a depth of $2\Delta Z$;

FIG. 33 illustrates the focus feedback signal $F[Z]$ for a 0.5NA system operating at wavelength λ = 0.633μm, with ΔZ = 0.5μm;

FIG. 34 illustrates a microlens layout with interspersed Z sensors;

FIGS. 35a,b are top and sectional side views of a system which provides six-axis micropositioning control of the microlens array, plus warp compensation; and

FIG. 36 shows a system-level schematic summarizing the various feedback and control mechanisms.

DESCRIPTION OF SPECIFIC EMBODIMENTS

Basic Principles of Operation

FIG. 1 illustrates a simple embodiment of the invention which could operate as a tandem scanning confocal microscope. The system contains a low-resolution, double-telecentric optical projection system 1 which images a microlens array 2 onto an optical detector array 3, with each microlens element being imaged onto a corresponding light-sensing detector element (e.g., microlens 4 is imaged onto detector element 5). Each individual microlens images a corresponding focal point at or near the sample surface 6 onto the projection system's aperture stop 7, so the corresponding detector element senses the sample reflectivity over a small microspot at the microlens's focal point (e.g., microlens 4 images point 8 onto the projection aperture 7, so element 5 senses the reflectivity at point 8). The sample is illuminated in reflection mode from an illumination system 9. The microspots are selectively illuminated by passing the illumination through the projection aperture 7 and microlens

array 2, using a beam splitter 10 to merge the illumination into the light path.

The diffraction-limited images of the projection aperture through the microlenses define the microspots, which are at least an order of magnitude smaller than the microlens aperture dimension. The microspots would preferably be comparable in size to the microlenses' diffraction point spread function. Thus, in the preferred embodiments the projection aperture performs the same function as the pinhole in a confocal microscope. One difference between this system and prior-art tandem scanning confocal microscopes is that instead of imaging an array of pinholes through a single objective, the system uses a single "pinhole" (i.e., the projection aperture) which is imaged through an array of "objectives" (microlenses).

FIG. 2 illustrates an embodiment which is very similar to the microscopy system of FIG. 1, but which could function as a lithography printer. (In this figure as well as later figures, elements corresponding to those in an earlier figure will generally be denoted with the same reference numeral.) This system also contains a low-resolution, double-telecentric projection system 1, but in this embodiment the projection system functions to focus an image source 11 onto the microlens array 2. The image source comprises an array of light-modulating source elements (e.g., spots or pads of variable reflectivity), with each source element being imaged onto a corresponding microlens element. The image source could be a Digital Micromirror Device (or DMD, Ref. 3), with each source element comprising an individual micromirror pixel element. Each microlens images the projection aperture 7 onto a corresponding microspot on the printing surface 12, and each source element controls the exposure level over the corresponding microspot. The image source 11 is illuminated in reflection mode from the illumination system 9, using a beam splitter 13 to merge the illumination into the light path.

This system differs in a couple of respects from the microlens photolithography invention of Hugle et. al. (Ref's. 4, 5). Hugle's system does not use a single projection aperture for the entire microlens array (as illustrated in FIG. 2), but rather comprises an array of microlens units with separate, parallel optical paths. Also, Hugle's microlenses are non-scanning, wide-field imaging devices, each covering an image field comparable in size to the microlens aperture dimension. In contrast, the

present invention uses a scanning technique to achieve full-field coverage with microlenses whose instantaneous image fields (i.e. the microspots) are at least an order of magnitude smaller than the microlens apertures. (As with the confocal microscope embodiment, the lithograhy system's microspots are defined by the diffraction-limited images of the projection aperture through the microlenses, and would preferably be comparable in size to the microlenses' diffraction point spread function.)

FIG. 3 illustrates a variant of the lithography system which combines the printing and microscopic imaging functions in a single device. This is similar to the FIG. 2 system, except that reflected light from the printing surface 12 is split out of the light path by the beam splitter 13 and directed onto an optical detector array 14. (A typical system might use two wavelengths such as a UV wavelength for exposure and a HeNe laser wavelength for imaging.) The detector could sense alignment marks on the printing surface, and it could take advantage of the accurate depth discrimination of confocal imaging to sense focus height variations across the surface. The position information would be used by a closed-loop servomechanism to control registration alignment and/or focus and tilt. The servomechanism could also correct for warp distortion in either the printing surface or the microlens array by applying a compensating stress distribution around the array's periphery.

In each of the above embodiments the sample or printing surface is scanned so that the microlenses' focal point array traces out a complete raster image. (Alternatively, the microlens system itself could be scanned relative to a fixed sample or printing surface.)

FIGS. 4-6 illustrate several alternative scan patterns that could be used, including the bi-directional raster scan (FIG. 4), continuous line scan (FIG. 5), and segmented line scan or "multiscan" (FIG. 6). With the bi-directional raster scan (FIG. 4) the image surface is divided into an array of square or rectangular cells with cell dimensions matching the microlens center spacing, and the surface is scanned bi-directionally so that each focal point 15 scans a pattern of raster lines covering a single cell 16. With the continuous line scan (FIG. 5) each focal point 17 scans just one raster line 18 extending across the entire image field. The microlenses are arranged in rows that are skewed relative to the scan direction 19 by a small angle δ so that the focal points trace out a pattern of closely-spaced raster lines, i.e.,

with the raster line period d_r being much smaller than the microlens center spacing d_m. ($d_r = d_m \sin\delta$.) The segmented line scan (FIG. 6) is similar, except that each raster line is divided into a number of segments (e.g., segments 20 and 21) that are scanned by different lens foci (e.g., 22 and 23).

The "multiscan" imaging mode is similar to the segmented scan (FIG. 6), except that the scan segments overlap so that each raster line is scanned more than once. Multiscan imaging could have a variety of uses. One application would be to create color images or prints by varying the illumination chromaticity between successive scans. (For example, line segment 20 in FIG. 6 would be scanned first by lens focus 22, and then again by focus 23 with different illumination.) A microscope system could use also use multiscan imaging to create three dimensional images by tilting the microlens array slightly relative to the scan direction so that successive image scans are acquired at slightly different focal depths. (Alternatively, rather than tilting the microlens array, a distribution of focal plane heights could be designed into the array.) In a lithography system, the illumination brightness could be varied between successive scans in order to provide control of the exposure dose. (This would be useful if the image source does not provide gray level control. With N scans, each at a different illumination level, the total number of possible exposure dose levels is 2^N.) Alternatively, a lithography system might use redundant scanning simply to minimize statistical imaging errors due to factors such as microlens defects.

The microlens scanner design principles, components, and subsystems will be described in greater detail below, with the primary emphasis being on microlithography and semiconductor wafer production. (Much of the specification applies directly to microscopy and other applications, however.) A practical embodiment of the microlithography system might use a continuous deep-UV laser light source such as a frequency-quadrupled 266nm Nd:YAG laser (Ref. 6) and a DMD image source similar to a prototype device that has been demonstrated with about 2,000,000 pixels (Ref. 3). The DMD is capable of operating at a frame rate of over 10 kHz, resulting in a pixel rate of $2 \cdot 10^{10}$ pixels/sec. Assuming a raster line period of about 0.1 micron the exposure area rate would be 2 cm^2/sec. The system could use a catadioptric projection optics system whose simple, compact design would make it possible to combine

multiple microlens scanner units in one machine, resulting in a total throughput on the order of 10 cm^2/sec.

Microlens Imaging Theory and Technique

The basic imaging characteristics of microlens arrays can be derived using methods of Fourier optics. (This assumes a small numerical aperture with insignificant optical aberrations, but these methods can nevertheless provide a useful first approximation to the properties of microlenses with numerical aperture of about 0.5 or less.)

We will denote by (X, Y) a microlens's focal plane field coordinates, and by (X', Y') its aperture plane coordinates (FIG. 7). The analysis will be simplified by introducing dimensionless field coordinates (x,y) and aperture coordinates (x',y'):

$$x = X/\lambda, \quad y = Y/\lambda \qquad \text{Eq 1}$$

$$x' = -X'/F_m, \quad y' = -Y'/F_m \qquad \text{Eq 2}$$

where λ is the exposure wavelength and F_m is the microlens focal length (FIG. 7). The(scalar) electric field amplitude distribution on the focal plane will be denoted as $A[x, y]$, and the electric field distribution on the microlens aperture plane will be denoted as $A'[x', y']$. (Note: Square brackets "[...]" are used here as function argument delimiters; round brackets "(...)" are used for grouping.) Ignoring an insignificant phase factor, A and A' are related approximately by a Fourier transform relationship:

$$A'[x',y'] = \int\int A[x,y]\exp[i2\pi(xx'+yy')]\,dx\,dy \qquad \text{Eq 3}$$

$$A[x,y] = \int\int A'[x',y']\exp[-i2\pi(xx'+yy')]\,dx'\,dy' \qquad \text{Eq 4}$$

(An electric field time separation factor of $\exp[+i\omega t]$ is assumed, and all integrals are taken from $-\infty$ to ∞.) The instantaneous energy distribution produced at the focal plane is proportional to $|A[x, y]|^2$. (This assumes that there is no significant overlap between distributions from adjacent microlenses, which is a safe assumption because the microlenses' center spacing would typically be over an order of magnitude larger than the diffraction-limited spot size.) If the spots are "flash exposed" using a pulsed light source (such as an excimer laser) the total exposure dose $E[x, y]$ after completing an entire scan will be an incoherent

superposition of diffraction-limited, overlapping microspot distributions laid out on a grid pattern:

$$E[x,y] = \sum_{j,k} g_{jk} \left| A[x - js, y - ks] \right|^2 \qquad \text{Eq 5}$$

where s is the grid size (in wavelength units) and g_{jk} is the exposure gray level (on a scale of 0 to 1) at point $(x, y) = (js, ks)$. If a continuous light source is used there would be some smearing of the microspots due to motion of the wafer while each spot is being exposed, but this "point smearing" effect is neglected here. The image would typically be exposed using a grid size s equal to the raster line period d_r (FIG. 5), or some multiple thereof, normalized to the wavelength:

$$s = m\, d_r / \lambda \qquad \text{Eq 6}$$

where m is an integer.

Three exposure distributions are of primary importance in microlens imaging: the point distribution $E_{point}[x, y]$ which is obtained when point $(x, y) = (0, 0)$ is exposed at unit gray level and all other points are unexposed, the line distribution $E_{line}[x, y]$ which is obtained when all grid points on the line $x = 0$ are exposed at unit gray level and all others are unexposed, and the plane distribution $E_{plane}[x, y]$ which is obtained when all grid points are exposed at unit gray level.

$$E_{point}[x,y] = \left| A[x,y] \right|^2 \qquad \text{Eq 7}$$

$$E_{line}[x,y] = \sum_{k=-\infty}^{\infty} \left| A[x, y - k\, s] \right|^2 \qquad \text{Eq 8}$$

$$E_{plane}[x,y] = \sum_{j=-\infty}^{\infty} \sum_{k=-\infty}^{\infty} \left| A[x - j\, s, y - k\, s] \right|^2 \qquad \text{Eq 9}$$

A fundamental result from Fourier optics is that if the grid size is within the limit

$$s < 1/(2\, NA_m) \qquad \text{Eq 10}$$

where NA_m is the microlens numerical aperture, then $E_{plane}[x, y]$ reduces to a constant and $E_{line}[x, y]$ has a uniform cross section in x (i.e., it has no y dependence):

the disjunctive composition of two positive line patterns (indicated by opposite hatching). In FIG. 13 two parallel, overlapping sets of positive line patterns are conjunctively composited to form narrow spaces. Multiple sets of such patterns could be interleaved to form high-density arrays of very small features with the feature density exceeding the classical diffraction limit. (The feature size and density are primarily limited by the resist contrast and overlay accuracy.)

Aperture design

The basic design tradeoffs relating to aperture sizing and microlens spacing are illustrated schematically in FIG. 14. Each microlens 31 focuses the beam down to a diffraction-limited focus spot with a tightly confined amplitude distribution $A[X, Y]$ on the wafer surface 12. This distribution is determined by the microlens's numerical aperture and by the amplitude distribution $A'[X', Y']$ over the microlens aperture 32. The latter distribution, which is the diffraction-limited image from the source element 33 corresponding to microlens 31, should preferably overfill the aperture 32 in order to optimize focus resolution on the wafer plane and also to minimize sensitivity of the focus spot to optical registration errors between the source elements and the microlens apertures. However, if the A' distribution is too broad (or if the microlenses are too closely spaced), it will also overlap adjacent microlens apertures 34 and 35, resulting in image cross-talk between adjacent apertures.

The A' distribution is determined by the projection system's numerical aperture and by the amplitude distribution $A''[X'', Y'']$ over the projection aperture 7. (A'' represents the portion of the aperture illumination that comes only from source element 33. The total aperture illumination field also includes similar distributions from all other source elements.) The source elements' aperture size can be chosen to optimally control the A'' distribution. If the source elements are much smaller than their center spacing then diffraction at element 33's aperture will cause the A'' distribution to be very evenly spread over the projection aperture 7, minimizing possible spreading or distortion of the projected image-plane distribution A' due to nonuniform aperture illumination. Also, sensitivity to misalignment of the illumination source can be minimized by making the source elements small. The

"negative." FIG. 10 illustrates constant-exposure contours at $0.25E_{plane}$, $0.5E_{plane}$, and $0.75E_{plane}$ for several positive line images of varying length constructed with $NA_m = 0.5$. (With a positive resist these patterns would develop into linear spaces.) The exposure points, indicated by "+" marks, are all exposed at unit gray level and are separated by 1.5λ in X and by λ in Y. Although the line and plane exposure theorems generally apply only to infinite lines and planes, short linear or rectangular features such as those in FIG. 10 could be formed with fairly straight contours and uniform cross sections. The straightness and uniformity could be improved by using gray level control and a small grid step (e.g., $s = 0.5$).

Simple image patterns such as those illustrated in FIG. 10 can be combined to create small, sharply detailed patterns by using "boolean compositing" operations. The simplest such operation is image reversal (i.e., boolean negation), which can be effected by gray level inversion, as described above. Other logical operations such as conjunction (logical AND) and disjunction (logical OR) could be effected by a multilevel processing procedure such as that illustrated in FIGS. 11a-f. In FIG. 11a a wafer substrate 24 is spin-coated with a thick PMMA layer 25, a planarized spin-on-glass (SOG) layer 26, and a thin resist layer 27 which is exposed and developed to create an etched pattern in the SOG. In FIG. 11b the top resist is stripped and a second PMMA layer 28, SOG layer 29, and thin resist 30 are applied, and the top resist is exposed and developed to create a second etched pattern in the top SOG layer. In FIG. 11c the double-layer PMMA structure is reactive ion-etched down to the substrate, resulting in an etch mask that exposes a region on the substrate defined by the conjunction of the etched areas on the two SOG layers.

In a variation of the above process the top PMMA is only etched far enough to expose the bottom SOG layer (FIG. 11d). This is followed by a selective etch which removes the top SOG layer and the exposed portion of the lower SOG layer (FIG. 11e), and finally the remaining PMMA is etched down to the substrate (FIG. 11f). This process results in an etch mask defined by the disjunction of the two SOG etch patterns.

FIGS. 12 and 13 show simple illustrations of boolean compositing. In FIG. 12 an array of small, square islands is created by

$$E_{line}[0] = E_{plane}\, s\, 16\, NA_m/(3\pi) \qquad \text{Eq 20}$$

From Eq 10 we obtain the following maximum limits on $E_{point}[0,0]$ and $E_{line}[0]$:

$$E_{point}[0,0] < E_{plane}\, \pi/4 \qquad \text{Eq 21}$$

$$E_{line}[0] < E_{plane}\, 8/(3\pi) \qquad \text{Eq 22}$$

FIG. 8 illustrates the point, line, and plane exposure profiles for NA_m = 0.5 and s = 1. (For smaller step sizes E_{point}/E_{plane} scales in proportion to s^2 and E_{line}/E_{plane} scales in proportion to s.

The plane exposure theorem implies a useful image reversal characteristic of microlens array scanners: If the illumination level is set so that the resist solubility threshold E_S is at $E_{plane}/2$, then image reversal can be achieved by simply inverting the image gray levels (i.e., substitute g_{jk} — 1-g_{jk} at each exposure point). For example, FIG. 9 illustrates the exposure profile (E vs X) for an image feature and its complement. The feature has an exposure profile E_a which is produced by the gray level distribution g_{jk}.

$$E_a[x,y] = \sum_{j,k} g_{jk} \left| A[x - j\,s, y - k\,s] \right|^2 \qquad \text{Eq 23}$$

Under image reversal, the exposure distribution E_a is transformed to distribution E_b = E_{plane}-E_a,

$$E_b[x,y] = \sum_{j,k} (1 - g_{jk}) \left| A[x - j\,s, y - k\,s] \right|^2 = E_{plane} - E_a[x,y] \qquad \text{Eq 24}$$

(from Eq 9). The two exposure profiles cross the solubility threshold E_S at the same points (since E_S = E_{plane}-E_S); hence they will develop to the same width dimension W. (If the image source provides gray level control, the image reversal process does not require that the solubility threshold E_S be at $E_{plane}/2$ because the positive and negative images' gray levels could be independently scaled so that any desired exposure contour is at E_S.)

Image features comprising closed contours enclosing high-exposure areas can be termed "positive," whereas the complementary features (closed contours enclosing low-exposure regions) can be termed

$$E_{plane} = \left(\iint |A[x,y]|^2 \, dx \, dy \right) / s^2 \qquad \text{Eq 11}$$

$$E_{line}[x] = \left(\int |A[x,y]|^2 \, dy \right) / s \qquad \text{Eq 12}$$

(These results, which we will respectively designate the "plane exposure theorem" and the "line exposure theorem," are derived in sections near the end of this description below. Note that with a positive resist the E_{plane} distribution will result in all the resist being dissolved, E_{line} will develop to an isolated linear space, and E_{point} will develop to an isolated hole.) Eq's 11 and 12 can alternatively be expressed in terms of aperture integrals instead of field integrals,

$$E_{plane} = \left(\iint |A'[x',y']|^2 \, dx' \, dy' \right) / s^2 \qquad \text{Eq 13}$$

$$E_{line}[x] = \left(\int \left| \int A'[x',y'] \exp[-i2\pi \, xx'] \, dx' \right|^2 dy' \right) / s \qquad \text{Eq 14}$$

For the special case of a uniformly-illuminated circular aperture, the aperture function A' has the form

$$A'[x',y'] = \begin{cases} A'_0 & \text{for } \sqrt{x'^2 + y'^2} < NA_m; \\ 0 & \text{otherwise} \end{cases} \qquad \text{Eq 15}$$

where A'_0 is a constant. Its inverse Fourier transform A has the form

$$A[x,y] = A'_0 \, NA_m \, J_1[2\pi \, NA_m \sqrt{x^2 + y^2}] / \sqrt{x^2 + y^2} \; . \qquad \text{Eq 16}$$

where J_1 is a Bessel function of the first kind. (Eq 16 represents the classical Airy diffraction pattern.) Substituting Eq's 15 and 16 in Eq's 7, 13, and 14, we obtain:

$$E_{point}[x,y] = E_{plane} \, s^2 \, J_1[2\pi \, NA_m \sqrt{x^2 + y^2}]^2 / \left(\pi (x^2 + y^2) \right) \qquad \text{Eq 17}$$

$$E_{line}[x] = E_{plane} \left(s / (NA_m \, \pi^3 \, x^2) \right) \left(1 - {}_1F_2[1; \tfrac{1}{2}, \tfrac{3}{2}; -(2\pi \, NA_m \, x)^2] \right) \qquad \text{Eq 18}$$

where ${}_1F_2$ is a generalized hypergeometric function. The peak values of these distributions are

$$E_{point}[0,0] = E_{plane} \, s^2 \, NA_m{}^2 \, \pi \qquad \text{Eq 19}$$

tradeoff, however, is that optical efficiency would fall off in proportion to the source elements' aperture size due to overfilling of the projection aperture.

The projection aperture size and shape can be designed to optimize the tradeoff between illumination uniformity across the microlens aperture 32 versus minimizing light leakage into adjacent apertures 34 and 35. One approach could be to use a square aperture 7 aligned to the microlens grid. The square-aperture amplitude transmittance function $t_p[X'', Y'']$ is

$$t_p[X'',Y''] = \begin{cases} 1 & \text{for } |X''| < W_p/2 \text{ and } |Y''| < W_p/2; \\ 0 & \text{otherwise} \end{cases} \qquad \text{Eq 25}$$

where W_p is the projection aperture width. Assuming that the A'' distribution is substantially uniform within the projection aperture, a square aperture will result in a microlens aperture distribution A' described approximately by the function

$$A'[X',Y'] = A'_0 \,\text{sinc}[W_p\, X'/(\lambda\, F_p)]\,\text{sinc}[W_p\, Y'/(\lambda\, F_p)] \qquad \text{Eq 26}$$

where A'_0 is a constant, F_p is the focal length of the optical subsystem between the projection aperture 7 and microlens aperture 32, λ is the exposure wavelength, and $\text{sinc}[u] = \sin[\pi u]/(\pi u)$. The aperture width W_p can be chosen so that the first nodes of the sinc function are approximately centered on the adjacent microlens apertures 34 and 35:

$$W_p = \lambda\, F_p / d_m \qquad \text{Eq 27}$$

where d_m is the microlens center spacing. In this case, Eq's 25 and 26 become:

$$t_p[X'',Y''] = \begin{cases} 1 & \text{for } |X''| < \lambda\, F_p/(2\, d_m) \text{ and } |Y''| < \lambda\, F_p/(2\, d_m); \\ 0 & \text{otherwise} \end{cases} \qquad \text{Eq 28}$$

$$A'[X',Y'] = A'_0 \,\text{sinc}[X'/d_m]\,\text{sinc}[Y'/d_m] \qquad \text{Eq 29}$$

If d_m is, for example, four times the microlens aperture width a_m (FIG. 14), the illumination intensity nonuniformity over the aperture 32 will be only about 5% (not enough to significantly impair focus resolution on the wafer plane) and the energy leakage into each adjacent aperture 34 or 35 will be about 0.4%, assuming circular microlens apertures.

The cross-talk amplitude component would not give rise to any significant coherence effects. For example, the primary amplitude distribution $A'[X', Y']$ over microlens aperture **32** is superimposed with cross-talk distributions $A'[X'+d_m, Y']$ and $A'[X'-d_m, Y']$ from adjacent source elements **34** and **35**. Each of the cross-talk distributions is approximately odd-symmetric in X' over aperture **32** whereas $A'[X', Y']$ is even-symmetric. This implies (based on the properties of Fourier transforms) that at the wafer plane the cross-talk amplitude will be approximately pure complex, whereas $A[X, Y]$ will be real-valued, resulting in minimal coherence interaction. This assumes that the illumination is coherent and that the source elements are coherently aligned. (If there are significant phase shifts between adjacent elements the cross-talk energy leakage could be much higher than the level indicated above, e.g., 0.4%, due to coherence interactions.)

There are variants of the square-aperture design outlined above that could result in even better cross-talk suppression. One alternative is to align the aperture at a 45° angle relative to the microlens grid and set its size so that *both* sinc terms in the A' distribution are zero at the center of adjacent microlens apertures **34** and **35**:

$$t_p[X'',Y''] = \begin{cases} 1 & \text{for } |X''+Y''| < \lambda F_p/d_m \text{ and } |X''-Y''| < \lambda F_p/d_m; \\ 0 & \text{otherwise} \end{cases} \quad \text{Eq 30}$$

$$A'[X',Y'] = A'_0 \,\mathrm{sinc}[(X'+Y')/d_m]\,\mathrm{sinc}[(X'-Y')/d_m] \quad \text{Eq 31}$$

Another approach is to use an apodized projection aperture which essentially replaces the square-aperture amplitude transmittance function of Eq 28 by its autoconvolution. With this modification the sinc functions in A' are replaced by sinc^2 terms, so over the adjacent apertures where A' has zero crossings the cross-talk amplitude becomes negligible:

$$t_p[X'',Y''] = \begin{cases} \left(1-\left|X''\, d_m/(\lambda F_p)\right|\right)\left(1-\left|Y''\, d_m/(\lambda F_p)\right|\right) \\ \qquad \text{for } |X''| < \lambda F_p/d_m \text{ and } |Y''| < \lambda F_p/d_m; \\ 0 \quad \text{otherwise} \end{cases} \quad \text{Eq 32}$$

$$A'[X',Y'] = A'_0 \,\mathrm{sinc}^2[X'/d_m]\,\mathrm{sinc}^2[Y'/d_m] \quad \text{Eq 33}$$

(These variant approaches have the disadvantage that either the illumination uniformity over the microlens aperture 32 would be compromised or the microlens spacing d_m would have to be increased to maintain illumination uniformity.)

The apodization approach can also be implemented by a slightly different technique. Rather than forming an actual physical apodizer at the projection aperture, the beam can be "effectively apodized" by designing the aperture illumination field A'' so that it has a tapered profile over the aperture region similar to an apodization profile. For example, if the illumination optics and image source are designed so that the A'' distribution's first diffraction nodes are at the projection aperture edges, the tapered amplitude distribution near the edges will tend to repress the diffraction tails in the image-plane distribution A'. (The tradeoff to this advantage, however, is that the system will be less tolerant of any misalignment or vibration that could cause the A'' distribution to shift.) Similarly, the microlens apertures could be effectively apodized by locating the first diffraction nodes of the A' distribution at the microlens aperture boundary. This would tend to repress the diffraction tails in the wafer-plane distribution A, though at the expense of increasing the central peak width.

The aperture design approaches outlined above can be applied to microscopy systems as well as lithography printers. (For the microscopy application the source elements 33 in FIG. 14 can be reinterpreted as detector elements.)

It should be noted that there is one application for which image cross-talk would not be a problem. If the system is used to print a periodic pattern, with the pattern periodicity matching the microlens layout, then the exposure intensities at all the microspots would be identical; so any cross-talk effect could be corrected by making a compensating adjustment in the overall exposure level. For this application an image source array would not even be required - it could simply be replaced by a modulated point source at the center of the projection aperture which would uniformly illuminate the entire microlens array. This type of system could be used, for example, in the manufacture of microlens arrays, wherein the image-plane microlens array would be used as a mastering element to lithographically pattern replica elements.

(However, an alternative manufacturing technique described below could have advantages over this method.)

Microlens Construction

FIG. 15 illustrates a possible configuration for the microlens design. Each microlens is formed as a surface relief profile **36** on the top surface of a thin fused silica plate **37**. A lithographically patterned light-blocking layer **38** such as dark chrome is deposited on the top of the plate to define the microlens apertures. The plate is optically contacted and bonded to a thick fused silica superstrate **39**. Portions of the superstrate's bottom surface are etched to form a light-scattering or diffracting surface **40** which represses the specular reflected beam over the optically contacted regions of the plate. The superstrate's top surface has an antireflection coatings **41**, and the bottom surface has an antireflection coating **42** over the microlens clear aperture areas. (The scattering or diffractive surface areas and the antireflection coatings prevent the specularly reflected light from transmitting back through the projection aperture.)

A fabrication process based on laser-assisted chemical etching (Ref's. 7, 8) is illustrated in FIGS. **16a-g**. The basic procedure is to first form an array of low-NA microlenses using a holographic construction process (FIGS. **16a-d**), and then to use this array as a mastering element for replicating arrays of accurately-profiled, high-NA microlenses (FIGS. **16e-g**). In FIG. **16a** a pair of accurately collimated, uniform laser beams **43** and **44** are combined to form an interference pattern which exposes a thick resist layer **45** on a fused silica substrate **46**. The substrate is then rotated 90° and exposed a second time, so the latent resist image consists of two orthogonal sets of uniformly-spaced parallel lines. The latent image is developed into a sinusoidal thickness variation in the resist (FIG. **16b**), which is converted to a sinusoidal surface profile **47** in the substrate by a reactive ion etching process (FIG. **16c**; Ref's. 7, 8). The surface height profile $Z[X, Y]$ consists of crossed sinusoids,

$$Z[X,Y] = Z_0\left(\cos^2[\pi X/d_m] + \cos^2[\pi Y/d_m]\right) \qquad \text{Eq 34}$$

where d_m is the holographic pattern's line period and Z_0 is a constant. The shape is approximately paraboloidal in the vicinity of the profile

peaks; for example near $(X, Y) = (0,0)$ the profile function takes the approximate form

$$Z[X,Y] \cong Z_0\left(2-(\pi/d_m)^2(X^2+Y^2)\right) \qquad \text{Eq 35}$$

These paraboloidal regions can function as microlens elements, and an aperture array **48** is formed on the surface to delimit these areas (FIG. **16d**). The aperture array is formed as a lithographically-patterned chrome layer which is holographically constructed using the exposure setup of FIG. **16a** to ensure accurate registration of the aperture array with the microlenses.

The low-NA microlens array can be used as a proximity mask for fabricating the high-NA array (FIG. **16e**). A thin fused silica plate **37** is optically contacted to a thick supporting substrate **49** and is overcoated with resist **50**. An exposure beam **51** is projected through the low-NA microlens array **46**, which focuses the beam onto an array of small spots on the resist (e.g., microlens **47** focuses the beam onto spot **52**). Each microlens images an optimal exposure distribution at its focal plane, resulting in an optimally-contoured surface profile in the developed resist. (The imaging optics will be described below.) The resist profile is transferred into the fused silica plate **37** by reactive ion etching, and a lithographically-patterned aperture array **38** is then formed on the surface (FIG. **16f**). (The low-NA microlens array **46** can also be used to lithographically pattern the aperture array.) Finally, the silica plate **37** is bonded to the superstrate **39** and is detached from the substrate **49** (FIG. **16g**).

The exposure optics used in the replication process (FIG. **16e**) is illustrated in FIG. **17**. An extended, diffuse light source **53** is focused by a projection system **54** onto the mastering element **46**. The projection system's aperture stop contains a gray-scale transmittance mask **55** which is imaged by each microlens **47** onto its corresponding exposure spot **52**. The mask's transmittance profile controls the resist exposure distribution, which in turn determines the replica microlenses' surface profile shape **36** (FIG. **15**). The substrate **49** and mastering element **46** are scanned across the beam during exposure (keeping their relative position fixed) in order to average out exposure nonuniformities due to factors such as the projection system's field nonuniformity and coherence effects. The projection system **54** should designed to be telecentric on the object

side so that the multiple images of the aperture mask 55 remain fixed relative to the resist 50 as elements 46 and 49 are scanned across the illumination field.

An advantage of the above fabrication method is that the uniformity and placement accuracy of the replica microlenses are not limited by the exposure tool's field uniformity or stepping accuracy - they are determined only by the uniformity and collimation accuracy of the exposure beams 43 and 44 used to fabricate the mastering element (FIG. 16a). Furthermore, the replica microlens arrays can be much larger than the exposure tool's image field.

Numerous alternatives to reactive ion-etched microlenses exist for either the mastering microlens elements or the replica array. Possibilities include molded microlenses, distributed-index planar microlenses, micro-Fresnel lenses (or binary optics), and melted-resin arrays (Ref. 9, Chap. 7). Although their material processing technologies differ, most of these microlens types are fabricated using photolithography, so the exposure techniques described above can be adapted to these alternative types as well. One practical variation of the above process, for example, would be to form the mastering microlenses 47 as distributed-index planar elements. The air space between the mastering element 46 and resist 50 (FIGS. 16e, 17) could then be replaced by a dielectric layer which is deposited over the mastering element 46. The replica microlenses would thus be formed by a contact printing process, rather than by proximity printing, which has the advantage that the critical air space tolerance requirement would be eliminated.

Projection and Illumination Optics

In the context of a lithography system (FIG. 2) the image source 11 defines the object plane of the projection system 1, and the microlens array 2 defines its image plane. The projection system should generally be telecentric on the image side since the optical axes of the individual microlenses will typically all be mutually parallel. If an image source such as a DMD is used the projection system should also be telecentric on the object side. The FIG. 2 configuration uses a collimating lens 56 to image the projection aperture 7 to infinity on the image side, and a collimating lens 57 is also used to image the aperture to infinity on the object side. An aperture lens (or lens system) 58

which contains the projection aperture 7 functions in conjunction with collimators 56 and 57 to image the image source 11 onto the microlens array 2. (The image source and microlens array could be positioned so that the collimators alone perform this imaging function, but a zero-power aperture lens 58 might still be needed for aberration control.)

The illumination system 9 in FIG. 2 contains an illumination aperture 59 which is imaged by a collimator 60, the beam splitter 13, and the projection optics onto the projection aperture 7. An alternative design configuration which simplifies the illumination optics is illustrated in FIG. 18. In this system the beam splitter 13 is incorporated within the aperture lens 58 and the projection aperture 7 and illumination aperture 59 are both formed directly on the beam splitter surface. Advantages of this system are that the beam splitter is very small and compact, and optical alignment is simplified because the apertures 7 and 59 are automatically aligned to each other.

An even simpler illumination system is illustrated in FIG. 19. Rather than using a beam splitter, the illumination is brought into the system by means of a small, off-axis source such as an optical fiber 60 adjacent to the projection aperture 7. (An optical corrector element such as a binary optic element might be incorporated in front of the fiber to balance off-axis aberrations.) The image source 11 must be designed to work with off-axis illumination in this configuration.

FIG. 20 illustrates a variant of the FIG. 19 configuration in which the two collimator lenses 56 and 57 are replaced by a single collimating mirror 61. A fold mirror 62 may be used to physically separate the microlens array 2 and wafer 12 from the projection optics. The projection aperture is a reflective element (e.g., a small, square reflective pad 63 deposited on a low-reflectance substrate 64) and the aperture lens 58 operates bidirectionally. An advantage of this configuration is that it would exhibit very little chromatic aberration and could hence be used with a fairly broadband (e.g., 10 nm bandwidth) illumination source. (The optical geometry can be designed so that the aperture lens 58 has essentially no power and functions only as an aberration-controlling element; hence its chromatic dispersion will be very small. Although the microlenses are high-NA refractive elements, their imaging performance is not much affected by chromatic dispersion because of their small size.)

The configuration illustrated in FIGS. **21a,b** is similar to FIG. **20**, except that it includes a confocal viewing system which is used as a position encoder to monitor wafer alignment and focus. (This system is functionally similar to the FIG. **3** system.) The encoder system would use a long-wavelength light source such as a 633nm HeNe laser which is outside of the sensitivity range of UV resists. The reflective pad **63** in this configuration (FIG. **21b**) comprises an optical coating which is highly reflective at the UV exposure wavelength, but is transparent at the encoder wavelength, and the substrate **64** is transparent at both wavelengths. (The coating should also be designed so that transmitted light at the encoder wavelength does not exhibit a significant phase discontinuity across the coating boundary.) A second optical coating **65** which is formed on the substrate's bottom surface functions as a beam splitter at the encoder wavelength. The encoder's viewing illumination **66** is projected through both coatings and merged with the UV light path. It then reflects off of the collimator **61** and fold mirror **62**, transmits through the microlens array **2**, and is reflected back from the wafer **12**. The return beam is partially reflected by the beamsplitter coating **65**, it again reflects off the collimator **61**, and is directed onto a detector array **14**. Due to its longer wavelength, the encoder system's optimum aperture size would be larger than that of the UV exposure system (e.g., see Eq 27 and FIG. **14**), so the beamsplitter coating **65** will have an aperture dimension larger than that of the UV-reflective pad **63**. The bottom surface of the substrate **64** is cut at a compound wedge angle so that the beam reflected from the bottom coating **65** is spatially separated from the UV beam reflected from the top coating **63**.

FIG. **21a** shows a top view of the system (as viewed through the collimator **61**), illustrating the positional relationships between the fold mirror aperture **62**, the image source **11**, and the detector array **14**. This represents only one possible configuration. The surface tilt on both the top and bottom of the substrate **64** can be independently chosen to position the apertures **62**, **11**, and **14** in any preferred arrangement within the area defined by the collimator aperture **61**. Also, the two reflective films could just as well be placed on the opposite sides of the substrate (i.e. with the UV-reflective film **63** on the bottom and the beam splitter coating **65** on top), although in this case the beam splitter coating would also have to be UV-transparent.

The Image Source

The Digital Micromirror Device (DMD, Ref. 3) has several favorable characteristics as an image source for microlithography: A digitally programmable image source would eliminate the need for lithography masks; the DMD's high frame rate (e.g., 10 kHz) should be sufficient to meet the throughput requirements for semiconductor production; and its pixel size (17μm center spacing) is small enough to allow unit magnification in the projection system.

A couple of tradeoffs must be properly balanced in the design of a DMD system. These tradeoffs relate to the micromirrors' aperture size requirement and surface form tolerance, the micromirror tilt range and tilt tolerance, energy efficiency, and image cross-talk. FIG. 22 illustrates a design configuration for the image source which uses an object-plane microlens array in conjunction with the micromirror array to optimally balance these factors. An off-axis illumination beam (such as that produced by the fiber illuminator 60 in FIG. 19) is focused by microlens array 67 to an array of points; e.g. the portion of the illumination beam 68 intercepting microlens 69 is focused to point 70. Each focused beam is intercepted by a micromirror which is tilted (when in its "on" state) to reimage the focus point to a diffraction-limited spot at the center of a microlens aperture adjacent to the focusing microlens; e.g. micromirror 71 reimages point 70 to a point 72 at the center of microlens 73 adjacent to microlens 69, and the projection optics then reimages point 72 onto the center of a corresponding aperture of the image-plane microlens array. The micromirrors may contain some built-in optical power to facilitate this imaging function. For example, element 71 in FIG. 22 is illustrated as having some convex curvature. (Alternatively, the micromirrors could be formed as binary optic reflectors. The optical power could also be provided by microlenses formed on the micromirror surfaces, or by separate, stationary microlenses positioned close to the micromirror apertures.)

In addition to imaging the illumination source onto the microlens apertures, the micromirrors and microlenses also function to image the microlens apertures onto the projection aperture. For example, point 74 at the center of microlens aperture 69 is imaged by micromirror 71 to a virtual image point 75, which is then imaged by microlens 72 (in

cooperation with the projection optics) onto the center of the projection aperture. (However, when the mirormirror is in its "off" position, as illustrated by element 76 in FIG. 22, it is tilted to divert the reflected beam 77 out of the projection aperture.)

A primary advantage of the above design configuration is that the uniform illumination over the object-plane microlens array 68 is effectively converted to an array of diffraction-limited point sources 72 in the reflected beam without incurring aperturing losses at the image source. This results in a controlled, even illumination distribution A" over the projection aperture and an image-plane distribution A' with minimal peak width (FIG. 14). The diffraction-limited size of the effective source points 72 is determined by the effective focal length of the microlens-micromirror combination (e.g. elements 69 and 71) and can be designed to optimize the tradeoff between image cross-talk suppression and energy efficiency. (Smaller source points will generally improve cross-talk suppression by reducing the width of the A' distribution, but will also result in a wider projection aperture distribution A" and consequent light loss due to overfilling of the aperture; see FIG. 14.)

Another advantage of the FIG. 22 configuration is that, by incorporating optical power in the micromirrors, the focal length of the object-plane microlenses can be reduced and the micromirrors can be positioned closer to the microlenses without incurring a wider spread of the projection aperture distribution A". This results in a more compact system and reduces the micromirror aperture size requirement (i.e. fill factor). (Even without incorporating optical power in the micromirrors, their apertures would only need to be half the size of the microlenses.) Furthermore, the surface figure tolerance and the micromirror tilt tolerance would also be relaxed, although these advantages would be balanced by an increased tilt range requirement and by the need to incorporate optical power in the microlenses.

The above design approach also has the advantage that it avoids the use of a beam splitter and the associated optical efficiency loss. Also, with the off-axis illumination arrangement there would be no need to tilt the projection system's object plane to accommodate the micromirror tilt.

The DMD is not the only option for the image source. One alternative, illustrated in FIG. 23, is to use a photomask 78 in

conjunction with an object-plane microlens array 79. (The microlenses could be binary optic elements.) The projection system 1 images the array 79 onto the image-plane microlens array 2 at reduced magnification. A dense array of image pixel elements comprising small pads of differing reflectivity is formed on the photomask surface. At any point in time some of the pixels will be positioned at the object-plane microlens foci positions (i.e. conjugate to the projection aperture) and will be illuminated in reflection mode through the microlenses. The image source elements comprise the object-plane microlenses and corresponding illuminated pixels, and the elements are modulated by scanning the photomask across the focal point array to bring different pixels into position at the focal points. "On" pixels are represented by bright chrome pads, and "off" pixels comprise transparent or absorbing areas. (A choice of gray levels could be provided by forming high-frequency etched gratings on the chrome pads.) The wafer 12 and photomask 78 are both synchronously scanned and the illumination source is strobed so that exposures are made when the microlens focal points on the mask are centered on the pixels. (A technique for effectively strobing the illumination without actually modulating the light source is discussed below.) Thus, the photomask's reflectivity distribution will be mapped onto a corresponding exposure distribution on the wafer at reduced size.

With conventional chrome-on-quartz photomasks, transmitted-light illumination generally results in higher-quality imaging than reflected-light illumination because transmitted light interacts less with the chrome sidewalls. However, this would not be the case with the microlens system because edge-scattered light is substantially eliminated by the projection aperture. Also, the pixels would be significantly larger than the diffraction-limited microlens foci so there will not be much edge scatter. For example, with a 10X reduction system which is designed to produce a 0.1μm microspot period on the wafer plane, the photomask pixel center spacing would be 1μm, whereas the pixel illumination spots would have a diameter (full width at first diffraction nodes) of only about 0.5μm (assuming deep UV illumination and a microlens NA of about 0.5). In addition to minimizing optical interactions with the chrome edges, the underfilled pixel apertures would provide some tolerance allowance for scanning synchronization error between the mask and the wafer.

If the image-plane microlenses are widely separated to suppress image cross-talk the photomask embodiment could incur severe optical losses because, unlike the DMD system (FIG. 22), the photomask system has no mechanism for concentrating the illumination within the object-plane microlenses. A good compromise between efficiency and cross-talk suppression can be achieved by using the "effective apodization" technique described above under "Aperture design": The object-plane microlens apertures and projection aperture are sized so that the first diffraction node of the amplitude distribution A'' on the projection aperture (FIG. 14) is approximately at the projection aperture boundary; and the image-plane microlens apertures are sized so that the first diffraction node of the image-plane distribution A' is approximately at the microlens aperture boundary. This arrangement would tend to minimize the diffraction tails at the image plane and could allow the microlens apertures to be spaced fairly closely without incurring significant image cross-talk.

The compromise between efficiency versus cross-talk suppression could be circumvented by using the microlenses as extended-field imaging devices rather than using confocal-mode point imaging. In this mode the microlenses and projection aperture would be scaled up in size so that the image-plane microlens apertures and microspots are are both much larger than the diffraction limit. (As in the confocal imaging mode, however, the microspots would be at least an order of magnitude smaller than the microlens apertures, so this system retains the advantage that the microlenses need only operate over a small angular field.) Due to the larger microlens aperture dimensions, it could be feasible to illuminate the photomask with transmitted light rather than using reflected light, so the system could use conventional photomasks and could use standard image enchancement techniques such as phase-shifting and annular illumination. (The term "microlens" may be a misnomer in this context because the lens apertures could actually be quite large, e.g. several millimeters in diameter.) This system could have advantages over conventional, monolithic stepper designs (e.g. compact, low cost optics), although it would lack some of the principal advantages of confocal imaging (superior lateral resolution and depth discrimination, insensitivity to geometric and chromatic aberrations in the lens array, less susceptibility to optical coherence effects).

Other types of image source mechanisms could also be used with the microlens scanner. For example, a reflective film strip might be used instead of a photomask. Although most of the device embodiments considered above use reflected-light illumination, transmitted light could potentially also be used. The image source could, for example, be a film transparency or a liquid crystal device (LCD). However, reflective media have the advantage that the illumination can be focused down to an array of very small pixel elements by means of an object-plane microlens array in close proximity to the light-modulating elements (as in FIGS. 22 and 23). Furthermore, transparent media such as film transparencies do not generally transmit deep UV illumination efficiently.

The Illumination Source

The catadioptric system illustrated in FIG. 20 would exhibit very little chromatic aberration, so it could possibly be used with a fairly wide-bandwidth (e.g., 10nm) illumination source such as a filtered arc lamp. This could be feasible for I-line (365 nm) processing, but for shorter wavelengths a deep UV laser source may be required to achieve sufficient exposure energy.

A pulsed laser such as a krypton fluoride (248 nm) or argon fluoride (193 nm) excimer laser could provide very high exposure energy. Line narrowing, which is required with conventional systems due to their high chromatic dispersion, would not be necessary with the catadioptric system. The pulse duration of an excimer laser is sufficiently short (e.g., 10 ns) that there would be no significant point smearing in the exposed image. The main drawback of excimer lasers is that their pulse repetition rate is typically less than 1kHz, which is much less than the DMD's achievable frame rate and probably too slow for the high throughput requirements of semiconductor production. This limitation could only be overcome by either greatly increasing the number of pixels in the DMD or by having multiple microlens scanner systems operating in parallel. (A single laser could perhaps supply illumination to several scanner units.)

The frame rate would not be limited if a continuous illumination source such as an arc lamp is used. For deep-UV applications a continuous-wave, frequency-quadrupled Nd:YAG laser (266 nm) may be an attractive option (Ref. 6). One problem that could be encountered with a continuous source is the image point smearing due to the relative motion

between the microlens array and the wafer. One way to reduce the smearing would be to effectively strobe the illumination by shuttering the light source, so that each image frame is exposed over a very brief time period. However this method would incur a very large loss in optical efficiency. Much of the loss could possibly be recovered by using the light source to supply several scanner units. (Rather than shuttering the light source, an optical switching mechanism would be used to sequentially cycle the illumination through several units.) However, in practice the illumination source may not have enough power to supply multiple units.

A practical solution of the point smearing problem would be to include a beam-scanning mechanism in the illumination optics which effectively strobes the beam by focusing the illumination to a narrow band, or a set of parallel bands, which are scanned at high speed across the image source. (Conceptually, this is analogous to the optical switching approach mentioned above, except that instead of switching the beam between different microlens scanner units it is effectively switched between different regions within a single unit.) This method is illustrated in FIGS. **24** and **25**.

FIG. **24** shows how the microlenses are positioned relative to the wafer exposure pattern using conventional, full-field illumination with a pulsed light source. The small circles (e.g., **80**) represent diffraction-limited microspots on the wafer, which are exposed at varying intensity levels to produce the raster image. The large circles **81** represent the microlens apertures, and the "+" marks **82** represent the positions of the microlens foci relative to the microspots at a particular instant in time. (In the context of the FIG. **23** system, FIG. **24** could alternatively be interpreted as representing the photomask **78**, where the circles represent the reflective pads and the "+" marks represent the foci of the object-plane microlenses **79**.) The wafer (or mask) is translated in the scan direction **19**, and the light source is pulsed when the foci are centered over the microspots.

FIG. **25** illustrates the exposure geometry using the scanned-illumination technique. The illumination is confined to a narrow band **83** (or set of parallel bands) which is scanned across the object and image fields in a direction **84** transverse to the band (or bands). The beam is scanned synchronously with the wafer scan so that each microlens focus passes over the center of a microspot during the time that it is

illuminated. (Note that in FIG. 25 the microlens foci outside of the illuminated area 83 are not centered on microspots, but the wafer scan will have shifted them to a centered position at the time they are traversed by the illumination beam.)

Positioning Feedback and Control

In the embodiments illustrated in FIGS. 3 and 21a,b the microlens array operates in conjunction with an optical detector array 14 as a position encoder which provides feedback to a closed-loop wafer positioning servomechanism. (A similar type of system could be used to control the photomask scanner in the FIG. 23 system.) The encoder data could include the wafer's lateral position (X and Y, where X is the scan coordinate and Y is the cross-scan coordinate), focus (Z), tilt (i.e., rotational displacements about the X and Y axes) and θ (rotation about the Z axis). In addition, the system could provide a measure of the surface warp distribution between the wafer and microlens array (i.e., Z as a function of X and Y). Typically, the position encoder would use a viewing wavelength different from the exposure wavelength, so the microlens array would need to include microlens elements that are specially designed for the encoder wavelength. (It may be possible, in principle, to design dual-wavelength microlenses. For example, a hybrid diffractive-refractive design could be used. However, the fabrication of such a design would be difficult and may entail performance compromises.) The encoder microlens elements could be formed as linear arrays bordering, or interspersed within, the two-dimensional array of exposure microlenses.

X-Y position sensing could be achieved by using a Moiré technique in which the confocal response of a periodic pattern of microlenses is measured on a periodic tracking pattern. The technique is illustrated in FIG. 26 for X tracking. A periodic row of microlenses L_0, L_1, L_2, ... with center spacing d_m is positioned over a periodic tracking pattern (such as an etched, rectangular-profile relief grating) with period d_t. The tracking position can be specified in terms of a parameter X_0 which is defined to be the X position, in wafer-based coordinates, of lens L_0's focus. (X_0 varies linearly with time.) The detector elements comprise light-sensing pixels, and the confocal response signal S_n at the pixel corresponding to lens L_n, as a function of the tracking position X_0 and pixel number n, satisfies the periodicity relationship

$$S_n[X_0] = S_0[X_0 + n\,d_m] \qquad \text{Eq 36}$$

The function S_0 is periodic modulo d_t,

$$S_0[X] = S_0[X \bmod d_t] \qquad \text{Eq 37}$$

The dimensions d_m and d_t are chosen so that d_m is close to, but not exactly equal to, an integer multiple of d_t,

$$d_m = k\,d_t + \delta \qquad \text{Eq 38}$$

where k is an integer and δ is a small value (significantly smaller than d_t). Thus,

$$S_n[X_0] = S_0[(X_0 + n(k\,d_t + \delta)) \bmod d_t] = S_0[X_0 + n\,\delta] \qquad \text{Eq 39}$$

The signal profile will shift by 1 pixel as the wafer moves by a distance of δ,

$$S_{n+1}[X_0] = S_0[X_0 + (n+1)\delta] = S_0[(X_0 + \delta) + n\delta] = S_n[X_0 + \delta] \qquad \text{Eq 40}$$

hence the pixel-resolution confocal response can be used to measure X_0 with a resolution of δ. Better resolution can be achieved by interpolating the detector signal between pixels. The interpolated detector signal (as a function of fractional pixel number n) will be periodic modulo d_t/δ, as illustrated in FIG. **27**:

$$S_{(n+d_t/\delta)}[X_0] = S_0[X_0 + (n + d_t/\delta)\delta] = S_0[X_0 + n\,\delta] = S_n[X_0] \qquad \text{Eq 41}$$

(from Eq's 39 and 37). The signal period d_t/δ is very large, so the detector signal's phase can be precisely measured to subpixel precision, resulting in a measurement precision of X_0 significantly better than δ.

In practice several sets of position-sensor microlenses may be provided for focusing at different heights. For example, FIG. **28** illustrates three interspersed microlens sets with different focus heights, h_1, h_2, and h_3. The microlenses may also be spherically corrected for focusing through different thicknesses of resist.

FIG. **29** illustrates a top view (looking down on the wafer plane) of a pattern that could be used for tracking X, Y, and θ rotation. Two parallel tracks are formed in the wafer scribe lines, each comprising parallel, etched wells **85** at 45° to the X-Y axes. The wells in one track are perpendicular to those of the other. A row of microlenses is disposed above each track. The microlens foci positions at a particular instant in time are indicated in FIG. **29** by "+" marks **86**. (The cross-sectional

geometry in an X-Z plane through either microlens row has the form described above and illustrated in FIG. 26 or 28.) Defining (X_0, Y_0) to be the wafer-based coordinates at one particular focus, the phase of the signal profile from each microlens row will be a function of both X_0 and Y_0, with one of the phase terms being proportional to X_0+Y_0 and the other proportional to X_0-Y_0. The sum of the two phase terms provides a measure of X_0, and the difference provides a measure of Y_0. Furthermore, any slight θ rotation will result in a measurable shift in the fundamental frequencies of the two signal profiles. One frequency will increase with θ, whereas the other will decrease, so the difference between the two frequencies can provide an accurate measure of θ. The sum of the two frequencies could also be monitored to detect any thermal expansion mismatch between the microlens array and the wafer. The tracking signal could be analyzed digitally, or analog electronics could be used to convert the tracking signal to a positioning control signal. The position feedback would be insensitive to minor defects or random inaccuracies in either the microlenses or the tracking pattern because the position measurement uses data from a large number of microlenses (e.g., 1000).

If the wafer stage has an encoder that is sufficiently accurate and precise, a much simpler tracking method could be used in which position feedback is simply provided by the stage encoder itself, rather than by the microlens encoder. However, it would still be necessary to accurately locate and align the wafer relative to the microlens array, and microlens imaging could be used for pre-exposure alignment. The alignment pattern could include large features for coarse positioning (e.g., a Gray-code bar pattern), plus a simple periodic line/space or checkerboard pattern to provide high-resolution X and Y measurement by the Moiré technique outlined above (FIGS. 26, 27). At least two sets of alignment patterns would be formed at widely-separated locations on the wafer to get good θ measurement accuracy.

Other X-Y alignment techniques are also possible. Rather than using the microlens array as a position-sensing element, a Moiré diffraction grating could be used (Ref. 10). Also, optical position encoder elements such as microlens arrays or Moiré diffraction gratings could be set directly into the wafer stage, and the alignment patterns could be formed on the wafer's back side. Several advantages of this approach are that the alignment patterns would not take up valuable wafer

space, they would not be affected by the wafer processing steps, and the close optical coupling between stage-embedded encoder elements and the wafer could help to improve alignment accuracy. A primary drawback of back-side alignment (and of top-side alignment using a Moiré grating) is that it does not provide a direct measure of the wafer position relative to the microlens array, so alignment would require accurate calibration of the *X-Y* offset between the array and the position encoders. (This disadvantage could perhaps be mitigated by performing all fabrication steps on each wafer using the same exposure tool. The positioning error related to the *X-Y* offset would then be the same on all process layers, and hence will not affect overlay accuracy.)

The wafer stage encoder may be capable of providing a sufficiently accurate and precise position feedback signal, but whether or not the system relies on the stage encoder as the primary positioning feedback sensor, the stage drive mechanism itself may not be able to provide adequately precise and responsive position control. High-inertia stage motors could provide smooth, uniform scanning motion with positioning accuracies at the submicron level, but to achieve alignment accuracies below the 0.1μm level while scanning the image at a frame rate of about 10 kHz additional alignment means may also be required.

Two supplementary fine-alignment mechanisms could be used, either alone or together. One would be a very precise *X-Y* position transducer, such as a piezoelectric actuator, coupled directly to the microlens array. If the microlens apertures are overfilled, slight lateral shifts in the microlens positions will simply cause their focal points to shift laterally without significantly affecting the focused spot intensity distribution. This mechanism would have a fast response time due to the microlens array's low inertia, but it would typically require an actuator with a resolution much better than 0.1μm. (If the microlens array does not itself function as the primary position feedback sensor, an additional *X-Y* position encoder would also have to be incorporated in the microlens system as part of the fine-alignment mechanism.) In the FIG. 23 embodiment this technique could also be used for *X-Y* fine alignment between the photomask **78** and object-plane microlens array **79**.

The second approach is to put an *X-Y* position actuator on the projection aperture. The focused spots on the wafer are diffraction-limited images of the projection aperture, so as long as the aperture is

sufficiently overfilled a translational shift of the aperture will induce a corresponding positional shift of the spots. The illumination optics could include a beam-steering mechanism which operates in synchronization with the aperture actuator to keep the illumination energy centered on the aperture. An advantage of this approach is that large positional adjustments of the aperture will translate to exceptionally fine-resolution shifts in the focused spot positions (e.g., a 1mm aperture shift might typically induce an image shift well below 0.1μm). Note that in the system configuration shown in FIGS. **21a,b** the UV exposure projection aperture and the viewing projection aperture are both formed on a common substrate **64**, so if the substrate position is adjusted for fine-alignment control the detector's X-Y feedback signal will always represent the wafer's relative position with the alignment correction applied. (This type of system would provide closed-loop alignment control. An alternative, open-loop design could be configured by depositing the UV aperture film **63** on a separate, movable substrate, while the viewing aperture film **65** remains fixed, so that the detector signal represents the relative wafer position before the fine-alignment correction is applied.)

The *X* alignment could also be fine-adjusted by synchronizing the image frame switching to the *X* encoder signal. For example, if the illumination source is an excimer laser its pulse switching could be triggered off of the encoder signal. Alternatively, if a DMD image source is used with a continuous light source, the frame rate could be synchronized to *X* by putting a variable time delay into the pixel switching or by phase-locking the DMD's clock signal to the encoder signal.

In addition to functioning as a positioning encoder for *X-Y* tracking or alignment, the microlens array could also function to measure focus error. The normalized confocal focus response $I[Z]$ of each microlens, as a function of focus position Z, has the form

$$I[Z] = \mathrm{sinc}^2[(4Z/\lambda)\sin^2[\alpha/2]] \qquad \text{Eq 42}$$

where λ is the wavelength, $\sin[\alpha]$ is the microlens numerical aperture, and $\mathrm{sinc}[u] = \sin[\pi u]/(\pi u)$ (Ref. 1; Eq 1.1 on p. 11). For example, FIG. **30** illustrates the confocal response of a 0.5NA system operating at wavelength $\lambda = 0.633\mu m$. The curve's full width at half max is 2.1μm. A very accurate measure of focus error can be obtained by comparing the

signal responses of two adjacent microlenses which have a slight relative offset in their focus curves. The offset could be designed into the microlenses; for example, FIG. 31 illustrates two focus-sensor microlenses 87 and 88 with their focal planes displaced respectively above and below the wafer surface 12 by a distance ΔZ.

A focus offset could also be created by positioning two parfocal microlenses over areas on the wafer with different etch depths. For example, FIG. 32 illustrates a configuration in which the focus-sensor microlenses 87 and 88 are designed to have a common focal plane displaced by a small distance ΔZ below the wafer surface, and portions of the wafer surface 12 (e.g., areas within the scribe lines) are etched to a depth of $2\Delta Z$. (Since the microlenses' focal lengths naturally tend to be greater at long wavelengths due to chromatic dispersion, this approach has the potential advantage that special-purpose focus-sensor lenses may not be required. The same lens set could be used to both focus the UV exposure points onto the top surface and focus 0.633 μm radiation below the top surface.) Using either approach (FIG. 31 or FIG. 32), one of the microlenses will have a confocal response $I[Z+\Delta Z]$ while the other's response will be $I[Z-\Delta Z]$. The two response functions can be combined to obtain a self-normalized focus feedback signal $F[Z]$ of the form

$$F[Z] = \frac{I[Z+\Delta Z] - I[Z-\Delta Z]}{I[Z+\Delta Z] + I[Z-\Delta Z]} \qquad \text{Eq 43}$$

This function is illustrated in FIG. 33 for a 0.5NA system operating at wavelength λ = 0.633μm, with ΔZ = 0.5μm. Within a +/-1.5μm range the function is monotonic and varies approximately linearly with focus position.

Generalizing on the concept illustrated in FIG. 31, three or more microlens sets covering a range of focal heights could be used to provide fine-focus capability over a large range of focus positions. (Or extending the FIG. 32 concept, three or more etch depths could be provided for extended-range focusing with parfocal microlenses.) Long focal length, low-NA microlenses could be used to provide coarse focusing over an even greater range, though the long-range focus elements would not have as good precision. (The focus range and precision error both vary in proportion to $1/NA^2$.)

In addition to measuring focus position, the relative tilt between the wafer and the microlens array can be measured by combining the output from three or more Z position encoders distributed at widely-separated positions on the array. A complete Z-height mapping over the array can also be made by combining the output from a large number of Z sensors. This data could be used to measure warp distortion.

One approach to warp measurement would be to use a row of Z sensors along the microlens array's leading edge to map out the wafer's warp distribution in raster fashion as the wafer is scanned under the array. However, this method would not provide information on the array's own intrinsic warp, which would have to be separately calibrated and added to the wafer warp get the cumulative warp distortion. The array's warp could be calibrated by measuring the exposure microlenses' confocal response on an optical flat (with UV illumination) over a range of focus heights. A simpler and more robust method for measuring warp might be to use several rows of Z sensor elements parallel to the leading-edge row and interspersed within the array. A microlens layout with interspersed Z sensors is illustrated in FIG. 34. This is similar to the multiscan layout in FIG. 6, except that Z sensor lenses (illustrated as the hatched circles) are interspersed along the scan lines. For example, adjacent scan lines 89 and 90 are covered by a Z sensor unit 91 comprising two or more microlenses 92 and 93 at the array's leading edge. These elements are designed for operation at the encoder viewing wavelength and have a built-in focus offset as in FIG. 31. (Ideally elements 92 and 93 would cover the same scan line, but they have a slight Y displacement in FIG. 34 so that the microlenses can be laid out in a square array.) This unit is followed by UV exposure lenses 94 and 95, a second Z sensor unit 96 and exposure lenses 97 and 98, etc. (In FIG. 34 one third of the lenses are shown as Z sensor elements, but in practice the ratio might be closer to 1% or less.)

The measured warp-induced focus error could be dynamically corrected by inducing a compensating warp distribution in the array. The corrective warp is generated by applying a stress distribution along the microlens array's periphery (e.g., by means of piezoelectric transducers). A very general warp distribution can be induced by this method. Over the array's interior there are no normal forces and the induced Z displacement

$\delta Z[X, Y]$, as a function of transverse coordinates X and Y, is described by the general thin-plate equilibrium equation,

$$\frac{\partial^4 \delta Z}{\partial X^4} + 2\frac{\partial^4 \delta Z}{\partial X^2 \partial Y^2} + \frac{\partial^4 \delta Z}{\partial Y^4} = 0 \qquad \text{Eq 44}$$

(from Ref. 11, Eq. 13.41 on p. 727). The solution of this equation is determined by the boundary values of δZ and its gradient; hence by controlling the surface height and gradient at the array periphery any warp distribution satisfying the above equation can, in principle, be generated. For example, a warp distribution having the form of a general third-order polynomial in X and Y could be induced.

The above technique could be implemented in practice as follows. Assume that there are Z sensors distributed within the microlens array's interior which provide focus height measurements Z_1, Z_2, ... relative to the wafer surface. Stress actuators, which are distributed around the array's periphery, are controlled by voltages V_1, V_2, ... Variations δV_1, δV_2, ... in the applied voltages will induce small focus height displacements δZ_1, δZ_2, ... which have an approximately linear dependence on the voltages,

$$\delta Z_i = \sum_j C_{ij}\, \delta V_j \qquad \text{Eq 45}$$

The C_{ij}'s are constant calibration coefficients which can be determined by focusing on an optical flat and measuring the induced warp distribution as various voltage combinations are applied. Eq 45 can be expressed in matrix notation as

$$\delta Z = C\, \delta V \qquad \text{Eq 46}$$

In the microlens array's operational mode, the focus heights Z_1, Z_2, ... are dynamically measured and subtracted from the design focus height (with compensation for any designed-in wafer topography) to obtain the computed height corrections δZ_1, δZ_2, ... Eq 46 can then be used to calculate the control voltage adjustments that will induce the computed correction. Eq 46 cannot generally be solved exactly because there may

typically be many more Z sensors than actuators, but the equation can be solved approximately by least-squares minimization:

$$\delta V = (C^T C)^{-1} C^T \delta Z \qquad \text{Eq 47}$$

where C^T is the matrix transpose of C. With some modification to provide damping of feedback oscillations, Eq 47 could serve as the basis of an algorithm to provide closed-loop control of fine focus, tilt, and warp compensation.

FIGS. **35a,b** are top and sectional side views of a system which provides six-axis micropositioning control of the microlens array, plus warp compensation. The microlenses are formed as an etched surface relief pattern on a very thin fused silica disk **37** (see FIG. **15**) which is bonded to a supporting fused silica superstrate **39**. The superstrate is disk-shaped and is thin enough to have some flexibility, and its bottom surface has a slight, shallow bevel **99** around its periphery to ensure wafer clearance as the disk is flexed. It is attached to a rigid, flanged tubular element **100** by means of vertically poled piezoelectric pads (e.g., **101** and **102**) which control the Z height distribution over the superstrate's periphery. The pads are distributed in a circumferential arrangement of paired elements, wherein the elements of each pair (e.g., elements **101** and **102**) are radially displaced so that they can act in opposition (e.g., one contracting, the other expanding) to control the superstrate's surface gradient at its periphery.

The outer surface of tubular element **100** has three flats on which piezoelectric shear plates (e.g., **103**) are bonded. The outer surface of each plate is bonded to a leaf spring (e.g., **104**) which is attached to a supporting outer tube **105**. Each piezoelectric plate is poled horizontally, parallel to the attached leaf spring, so the three plates can be actuated to provide X, Y, and θ micropositioning control. The outer tube **105** could be housed in a conventional microscope focus mechanism which is used for initial coarse-focus adjustment, but which would normally be locked during scan exposure operations.

FIG. **36** shows a system-level schematic summarizing the various feedback and control mechanisms described above, in a preferred embodiment. (A practical microlithography exposure tool would not necessarily require all of the elements illustrated in FIG. **36**.) Optical paths are indicated in the diagram by heavy, solid lines; electronic data

or signal paths are represented as light, solid lines; and mechanical control linkages are represented as dashed lines. The "controller" **106** may comprise one or more computers, digital micro-controllers, analog circuits, or a combination of such elements. The controller synchronizes the wafer scan, the DMD image frame generation, and (optionally) an illumination beam scanner **107** (see FIG. **25**); and it also controls a feedback loop which dynamically corrects scan positioning errors. The optical detector signal provides dynamic focus, tilt, and warp measurement during scanning, and also provides high-resolution X-Y and θ position data for pre-exposure alignment by the Moiré technique described above. The Moiré signal could possibly also be used for dynamic scan control, although it may be more practical to rely on the stage encoder **108** for fine X-Y scan position sensing. Coarse X-Y scan actuation would be provided by the stage motors **109**, while high-resolution X-Y scan positioning, as well as focus, tilt, and warp correction, would be provided by a piezoelectric actuator **110** coupled to the microlens array. (The piezoelectric servomechanism would have its own position encoder **111**.) Fine X-Y scan control could also optionally be provided by means of mechanical actuators **112** and **113** coupled to the projection and illumination apertures.

Notation for Derivation of Eq's 11 and 12

In the derivations below the following notational convenience will be used to represent a function f that takes arguments x, y, ...:

$$(f[x,\ y,\ \ldots]\ |\ x,\ y\ ,\ \ldots)$$

(The above expression is read "the function that, when applied to arguments x, y, ..., yields $f[x,\ y,\ \ldots]$".) Also, the Fourier transform of a function f will be denoted

$$\mathcal{F}[f] = (\int\!\ldots\!\int f[x,\ y,\ \ldots]\ \exp[i2\pi(xx'+yy'+\ldots)]\ dx\ dy\ldots\ |\ x',\ y',\ \ldots)$$

where $\mathcal{F}$ can represent the one-dimensional Fourier transform, or the two-dimensional transform, etc., depending on how many arguments f takes. This is the "unitary" form of the Fourier transform, which has a 2π factor

in the exponent. With this convention, the inverse transformation $\mathcal{F}^{-1}$ has the form

$$\mathcal{F}^{-1}[f] = (\int\ldots\int f[x', y', \ldots] \exp[-i2\pi(xx'+yy'+\ldots)]\, dx'\, dy'\ldots \mid x, y, \ldots)$$

The convolution operator, conv, is defined by

$$\text{conv}[f, g] = (\int\ldots\int f[x', y', \ldots]\, g[x-x', y-y', \ldots]\, dx'\, dy' \ldots \mid x, y, \ldots)$$

where this can represent the one-dimensional convolution, or the two-dimensional convolution, etc., depending on the type of f and g. We will also make use of the Dirac delta function δ, and the Dirac comb function, which is defined by

$$\text{comb}[x] = \sum_{j=-\infty}^{\infty} \delta[x-j]$$

Derivation of the Plane Exposure Theorem (Eq 11)

Eq 11 can be derived by using the following equivalent form of Eq 9

$$E_{plane} = \text{conv}[|A|^2, (\text{comb}[x/s]\ \text{comb}[y/s] / s^2 \mid x, y)] \qquad \text{Eq A1}$$

Taking the Fourier transform of both sides of Eq A1, applying the convolution theorem ($\mathcal{F}[\text{conv}[f,g]] = \mathcal{F}[f] \cdot \mathcal{F}[g]$), and making use of the relation $\mathcal{F}[\text{comb}] = \text{comb}$, we obtain

$$\mathcal{F}[E_{plane}] = \mathcal{F}[|A|^2] \cdot (\text{comb}[x's]\ \text{comb}[y's] \mid x', y') \qquad \text{Eq A2}$$

Again applying the convolution theorem ($\mathcal{F}[f \cdot g] = \text{conv}[\mathcal{F}[f], \mathcal{F}[g]]$), the first term on the right side of Eq A2 translates to

$$\mathcal{F}[|A|^2] = \text{conv}[A', (A'[-x', -y']^* \mid x', y')] \qquad \text{Eq A3}$$

The aperture function $A'[x', y']$ is zero everywhere outside of a square of half-width NA_m centered at the origin,

$$A'[x', y'] = 0 \quad \text{if} \quad |x'| > NA_m \quad \text{or} \quad |y'| > NA_m \qquad \text{Eq A4}$$

from which it follows that Eq A3 is zero outside a square of half-width $2\ NA_m$,

$$\text{conv}[A',\ (A'[-x', -y']^* \mid x', y')][x', y'] = 0$$
$$\text{if} \quad |x'| > 2\ NA_m \quad \text{or} \quad |y'| > 2\ NA_m \qquad \text{Eq A5}$$

But the comb term in Eq A2 consists of a superposition of delta functions located at points where x' and y' are integer multiples of $1/s$, so under the assumption that $s < 1/(2\ NA_m)$ (Eq 10) all of these delta functions except the zero-order term at $(x', y') = (0,0)$ will be masked by the aperture function:

$$\mathcal{F}[E_{plane}] = \mathcal{F}[|A|^2] \cdot (\delta[x's]\ \delta[y's] \mid x', y') \qquad \text{Eq A6}$$

Taking the inverse Fourier transform of both sides this expression, we obtain

$$E_{plane} = \text{conv}[|A|^2,\ (1/s^2 \mid x, y)] \qquad \text{Eq A7}$$

which is equivalent to Eq 11.

Derivation of the Line Exposure Theorem (Eq 12)

Eq 12 can be derived by using the following equivalent form of Eq 8:

$$(E_{line}[x, y] \mid y) = \text{conv}[(|A[x, y]|^2 \mid y),\ (\text{comb}[y/s]/s \mid y)] \qquad \text{Eq A8}$$

Taking the inverse Fourier transform of both sides of Eq A8 and applying the (1-dimensional) convolution theorem yields

$$\mathcal{F}[(E_{line}[x, y] \mid y)] = \mathcal{F}[(|A[x, y]|^2 \mid y)] \cdot (\text{comb}[y's] \mid y') \qquad \text{Eq A9}$$

Again applying the convolution theorem, the first term on the right side of Eq A9 translates to

$$\mathcal{F}[(|A[x, y]|^2 \mid y)] = \text{conv}[\mathcal{F}[(A[x, y] \mid y)], \mathcal{F}[(A[x, -y]^* \mid y)]] \quad \text{Eq A10}$$

The two-dimensional Fourier transform operation relating A to A' (Eq 3, $A' = \mathcal{F}[A]$) is equivalent to the composition of two one-dimensional Fourier transforms applied sequentially to the x and y coordinates,

$$A'[x', y'] = \mathcal{F}[A][x', y'] = \mathcal{F}[((\mathcal{F}[(A[x, y] \mid y)][y']) \mid x)][x'] \quad \text{Eq A11}$$

Hence, the Fourier transform of $A[x, y]$ with respect to just the y variable is equivalent to the inverse transform of $A'[x', y']$ with respect to x',

$$\mathcal{F}[(A[x, y] \mid y)][y'] = \mathcal{F}^{-1}[(A'[x', y'] \mid x')][x] \quad \text{Eq A12}$$

Since $A'[x', y'] = 0$ for $|y'| > NA_m$ (Eq A4) it also follows that

$$\mathcal{F}^{-1}[(A'[x', y'] \mid x')][x] = 0 \quad \text{for} \quad |y'| > NA_m \quad \text{Eq A13}$$

Hence, from Eq A12 both arguments of the convolution operator in Eq A10 will be zero outside an interval of half-width NA_m centered at zero, and therefore

$$\text{conv}[\mathcal{F}[(A[x, y] \mid y)], \mathcal{F}[(A[x, -y]^* \mid y)]][y'] = 0 \quad \text{for} \quad |y'| > 2\,NA_m \quad \text{Eq A14}$$

Under the assumption that $s < 1/(2\,NA_m)$ it follows from Eq A14 that all the delta functions constituting the comb term in Eq A9, except for the zero-order term, will be masked by the aperture function; hence Eq A9 is equivalent to

$$\mathcal{F}[(E_{line}[x, y] \mid y)] = \mathcal{F}[(|A[x, y]|^2 \mid y)] \cdot (\delta[y's] \mid y') \quad \text{Eq A15}$$

Taking the inverse Fourier transform of both sides of Eq A15, we obtain

$$(E_{line}[x, y] \mid y) = \text{conv}[(|A[x, y]|^2 \mid y), (1/s \mid y)] \quad \text{Eq A16}$$

which is equivalent to Eq 12.

Conclusion

In conclusion it can be seen that the present invention provides imaging systems and techniques for achieving high resolution and field size. Systems according to the invention can be readily manufactured using existing microlithographic and other optical technologies. The invention thus reduces the complexity and expense that characterize conventional wide-field, high-NA microscopy and microlithography systems. Furthermore, it provides potential performance advantages in that it makes possible flat field, distortion-free imaging, with accurate overlay, focus, and warp compensation, over very large image fields (larger than the practical limits of conventional imaging means). In one embodiment it would use a Digital Micromirror Device as the image source, potentially eliminating the need for photomasks in semiconductor manufacture.

While the above is a complete description of specific embodiments of the invention, various modifications, alternative constructions, and equivalents may be used. Therefore, the above description should not be taken as limiting the scope of the invention as defined by the claims.

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What is claimed is:

1. An imaging system comprising:

an optical projection system having an object plane, an image plane which is conjugate to the object plane, and a limiting aperture stop which is referred to as the projection aperture;

a planar array of microlenses having respective apertures defining a microlens aperture array, wherein the aperture array is positioned at the projection system's object plane, and wherein the microlenses have respective focal points which are conjugate to the projection aperture and which define a focal point array;

a scanning mechanism which establishes relative motion between the microlens array and an imaging sample proximate the focal point array, wherein the paths traversed by the focal points relative to the sample comprise a set of closely-spaced raster lines;

a detector comprising an array of light-sensing detector elements, wherein the detector is positioned at the projection system's image plane, and wherein the projection system images each microlens aperture onto a corresponding detector element and the detector element thus responds to light originating from a microspot on or in the sample, proximate the corresponding microlens focal point; and

a data acquisition system for recording the detector response as the scanning mechanism operates to establish relative motion between the sample and the microlens array, whereby a high-resolution raster image of the sample is synthesized.

2. The imaging system of claim 1, further comprising an illumination system, and wherein the microlens array and projection system are further configured to focus light from the illumination system onto the microspots to provide sample illumination.

3. The imaging system of claim 2, further comprising a beam splitter disposed to merge light from the illumination system into the projection system's light path so that the light, so merged, and the image light reflected from the sample traverse the same optical path between the beam splitter and the sample.

4. The imaging system of claim 1 wherein the microlenses all have the same focal length and their focal points are all in a common focal plane which is parallel to the scan direction, whereby the system achieves high resolution imaging at a selected focal depth on or in the sample.

5. The imaging system of claim 2, further comprising a mechanism for altering the illumination chromaticity concurrently with the scanning motion, wherein each raster line is scanned by multiple microlenses and multicolor or multiple-wavelength imagery is synthesized from the successive scans.

6. The imaging system of claim 1, wherein each raster line is scanned by multiple microlenses having different focal lengths, and three-dimensional image information is synthesized by combining images scanned at different focal depths on or in the sample.

7. The imaging system of claim 1 wherein:

each raster line is scanned by multiple microlenses;

the microlenses all have the same focal length and their focal points are all in a common focal plane which is tilted relative to the scan direction; and

three-dimensional image information is synthesized by combining images scanned at different focal depths on or in the sample.

8. A printing system comprising:

an optical projection system having an object plane, an image plane which is conjugate to the object plane, and a limiting aperture stop which is referred to as the projection aperture;

a planar array of microlenses having respective apertures defining a microlens aperture array, wherein the aperture array is positioned at the projection system's image plane, and wherein the microlenses have respective focal points which are conjugate to the projection aperture and which define a focal point array;

a scanning mechanism which establishes relative motion between the the microlens array and a printing surface proximate the focal point

array, wherein the paths traversed by the focal points relative to the printing surface comprise a set of closely-spaced raster lines;

an image source comprising an array of light-modulating image source elements, wherein the image source is positioned at the projection system's object plane, and wherein the projection system images each image source element onto a corresponding microlens aperture and the image source element thus controls the light level over a microspot on the printing surface, proximate the corresponding microlens focal point; and

an image modulation mechanism that controls the image source as the printing surface is scanned, whereby, when a photosensitive material is positioned in the printing surface, a synthesized, high-resolution raster image is recorded on the photosensitive material.

9. The printing system of claim 8 wherein the photosensitive material is photoresist on a planar substrate.

10. The printing system of claim 9 wherein the substrate is a semiconductor wafer.

11. The printing system of claim 8 wherein the projection aperture size and shape are determined so that the diffraction-limited amplitude distribution produced by each image source element on its corresponding microlens aperture has nodes on adjacent microlens apertures, whereby light leakage into adjacent microlenses is minimized.

12. The printing system of claim 8 wherein the projection aperture is apodized to minimize light leakage into adjacent microlens apertures.

13. The printing system of claim 8, further comprising an illumination system which illuminates the image source, wherein the illumination is modulated by the image source elements and is transmitted by the projection system and microlens array onto the printing surface.

14. The printing system of claim 13 wherein:

the scanning mechanism of claim 8 defines a first scanning mechanism, and the illumination system further comprises a second scanning mechanism;

the illumination system illuminates only a narrow band, or set of parallel bands, on the image source and on the microlens array at any particular instant in time; and

the second scanning mechanism repeatedly scans the illumination band or bands across the image field in synchronization with the first scanning mechanism so that each microspot is only illuminated during a very brief time interval during which it is traversed by an illumination band, therby minimizing smearing of the exposure pattern on the printing surface due to the relative motion between the printing surface and the microlens array.

15. The printing system of claim 13 wherein the image source comprises a light-transmitting optical medium, the illumination system illuminates the image source in transmission mode, and the image source elements comprise respective zones on the optical medium having differing optical transmittance characteristics.

16. The printing system of claim 13 wherein the image source comprises a light-reflecting optical medium, the illumination system illuminates the image source in reflection mode, and the image source elements comprise respective zones on the optical medium having differing optical reflectance characteristics.

17. The printing system of claim 16 wherein the image source comprises a digital micromirror device (DMD) and the projection system is telecentric on the object side.

18. The printing system of claim 16, further comprising a beam splitter disposed to merge light from the illumination system into the projection system's light path so that the light, so merged, and the image light reflected from the image source traverse the same optical path between the beam splitter and the image source.

19. The printing system of claim 16 wherein the illumination system comprises an off-axis illumination source adjacent the projection aperture.

20. The printing system of claim 19 wherein the illumination source comprises a fiber optic illuminator.

21. The printing system of claim 19 wherein:

the microlens array of claim 8 defines a first microlens array;

the image source further comprises a digital micromirror device (DMD), and a second microlens array disposed proximate the DMD;

each image source element comprises corresponding first and second microlenses of the second microlens array and a corresponding micromirror of the DMD;

the projection system is telecentric on the object side;

the second microlens array is disposed in the projection system's object plane;

each image source element's corresponding first microlens focuses the illumination source to a corresponding first illumination image point proximate the corresponding micromirror;

each image source element's corresponding micromirror has tilt control and built-in optical power so that, when the micromirror is in its "on" state,

the corresponding first illumination image point is reimaged by the micromirror to a corresponding second illumination image point at the center of the corresponding second microlens's aperture, and

the corresponding first microlens's aperture is imaged by the micromirror to a corresponding aperture image proximate the micromirror;

each image source element's corresponding second illumination image point is reimaged by the projection system onto the corresponding microlens aperture of the first microlens array;

each image source element's corresponding second microlens images the corresponding aperture image onto the projection aperture; and

each image source element's corresponding micromirror is tilted, when in its "off" position, to divert the illumination light intercepted by the corresponding first microlens out of the projection aperture;

wherein the optical power in the DMD micromirror elements and in the second microlens array elements, and the separation distance between the DMD and the second microlens array, are selected to balance the tradeoffs relating to the micromirrors' aperture size requirement and surface form tolerance, the micromirror tilt range and tilt tolerance, energy efficiency, and image cross-talk.

22. The printing system of claim 8 wherein:

the microlens array, the microlens aperture array, and the focal point array of claim 8 respectively define a first microlens array, first microlens aperture array, and first focal point array;

the image source further comprises a second planar array of microlenses having respective apertures defining a second microlens aperture array;

the second microlens aperture array is positioned at the projection system's object plane;

the microlens elements of the second microlens array have respective focal points which are conjugate to the projection aperture and which define a second focal point array; and

each image source element comprises a respective microlens of the second microlens array and a light-modulating element positioned at the respective microlens's focal point.

23. The imaging system of claim 22, further comprising an illumination system and a reflective surface positioned at the second focal point array, and wherein:

the illumination system illuminates the image source in reflection mode;

the light-modulating elements comprise spots of variable reflectivity on the reflective surface at the focal point locations of the second focal point array; and

the second microlens array and projection system are further configured to focus light from the illumination system onto the reflective spots.

24. The printing system of claim 23 wherein the reflective surface comprises a photomask which operates in reflection mode, and the light-modulating elements' reflectivities are varied by translating the photomask across the second focal point array so that different portions of the photomask with different optical reflectance characteristics are brought into position at the focal points of the second focal point array as the printing surface is scanned.

25. The printing system of claim 8 wherein the projection system is double-telecentric.

26. The printing system of claim 25, wherein the projection system comprises a first collimating lens element that images the projection aperture to infinity on the object side of the projection system, thereby making the system telecentric on the object side, and a second collimating lens element that images the projection aperture to infinity on the projection system's image side, thereby making the system telecentric on the image side.

27. The printing system of claim 25 wherein the projection system comprises:

a collimating mirror having first and second off-axis portions; and

a reflector in the projection aperture;

wherein

the first off-axis portion of the collimating mirror images the projection aperture to infinity on the object side of the projection system, thereby making the system telecentric on the object side;

the first off-axis portion reflects light from the object plane toward the projection aperture;

the reflector in the projection aperture reflects the light from the first off-axis portion back onto the collimating mirror on its second off-axis portion;

the second off-axis portion reflects the light from the projection aperture onto the image plane; and

the second off-axis portion images the projection aperture to infinity on the image side, thereby making the system telecentric on the image side.

28. The printing system of claim 8, further comprising an optical detector and positional feedback control mechanism, wherein:

the microlens array and projection system not only focus light from the image source onto the printing surface, but also collect a reflected beam comprising optical energy reflected from the printing surface and project it onto the optical detector, thereby producing a detector signal which provides information on the positional relationship between microlens array and the printing surface; and

the positional information is used by the feedback control mechanism to accurately control the positional relationship.

29. The printing system of claim 28, further comprising a beam splitter disposed to separate the reflected beam from the projection system's light path, wherein the light projected onto the printing surface and the reflected light traverse the same optical path between the beam splitter and the printing surface.

30. The printing system of claim 29 wherein the printing surface is illuminated by two wavelengths or narrow spectral ranges of wavelengths, a first wavelength which exposes the photosensitive material, and a second wavelength which is sensed by the detector to provide positional information.

31. The printing system of claim 30 wherein the projection system is double-telecentric.

32. The printing system of claim 31 wherein the projection system comprises:

a collimating mirror having first and second off-axis portions; and

a reflector in the projection aperture;

wherein

the first off-axis portion of the collimating mirror images the projection aperture to infinity on the object side of the projection system, thereby making the system telecentric on the object side;

the first off-axis portion reflects light at the first wavelength from the object plane toward the projection aperture;

the reflector in the projection aperture reflects the light from the first off-axis portion back onto the collimating mirror on its second off-axis portion;

the second off-axis portion reflects the light from the projection aperture onto the image plane; and

the second off-axis portion images the projection aperture to infinity on the image side, thereby making the system telecentric on the image side.

33. The printing system of claim 32 wherein:

the collimating mirror further comprises a third off-axis portion;

the aperture reflector further comprises a first optical coating which is deposited on a transparent wedge substrate, and which exhibits high reflectivity at the first wavelength, but which is transparent at the second wavelength;

the beam splitter comprises a second optical coating which is deposited on the wedge, on the surface opposite that of the first coating;

the second coating is partially reflective at the second wavelength;

illumination energy at the second wavelength is projected from a light source through both coatings, toward the second off-axis portion of the collimating mirror, so that both wavelengths traverse the same optical path between the wedge and the printing surface;

the beam reflected back from the printing surface at the second wavelength is partially reflected by the second coating toward the third off-axis mirror portion, which is spatially separated from the first off-axis portion due to the wedge angle between the two coatings; and

the third off-axis mirror portion then reflects the beam onto the detector.

34. The printing system of claim 28 wherein:

the printing surface further comprises positioning alignment marks that are detected by the positional feedback control mechanism and are used to determine a component of the positional relationship defined by the microlens array's and printing surface's lateral positional relationship parallel to the microlens array; and

the positional information is used to accurately control the lateral positional relationship and to synchronize the scanning mechanism with the image source.

35. The printing system of claim 34 wherein the alignment marks and focal point array comprise periodic patterns, with the periodicity of the alignment marks differing from that of the focal point array so that the reflected energy from the alignment marks forms a Moiré pattern in the detector signal which provides an accurate and precise measure of the lateral positional relationship between the microlens array and the printing surface.

36. The printing system of claim 28 wherein the projection aperture greatly attenuates out-of-focus light from the microlenses so that the detector signal comprises a focus signal that provides an accurate and precise measure of the microlens array's focus height relative to the printing surface, and wherein the focus signal is used by the positional feedback control mechanism to accurately control the focus height.

37. The printing system of claim 36 wherein the focus height is detected at one or more positions on the printing surface, and wherein the focus height at each position is detected by comparing the reflected energy signals from two or more microlenses which are focused on proximate points on a flat area on the printing surface, but which have different focal lengths so that the differential detector signal from the microlenses provides a sensitive measure of focus height.

38. The printing system of claim 36 wherein the focus height is detected at one or more positions on the printing surface, and wherein the focus height at each position is detected by comparing the reflected

energy signals from two or more microlenses which have the same focal length, but which are focused on proximate points straddling a step or steps on the printing surface so that the differential detector signal from the microlenses provides a sensitive measure of focus height.

39. The printing system of claim 38 wherein:

the focus steps are recessed wells in the printing surface, and the printing surface comprises a top surface outside of the focus wells and a bottom surface at the bottom of the focus wells;

the photosensitive material is disposed on the top surface;

the printing surface is illuminated by two wavelengths or narrow spectral ranges of wavelengths, a first wavelength which exposes the photosensitive material, and a second wavelength which is sensed by the detector to provide the focus signal; and

the focus signal is obtained from microlens elements that are used for the dual purposes of printing and focus sensing, but wherein their focal length at the second wavelength is longer than at the first wavelength due to chromatic dispersion, whereby the microlens array can be positioned to focus the first wavelength onto the top surface while simultaneously focusing the second wavelength onto a focal plane between the top and bottom surfaces to achieve good focus signal resolution.

40. The printing system of claim 8, further comprising a two-axis positioning transducer that continuously adjusts the projection aperture's lateral position parallel to the projection aperture plane to correct for small errors in the microlens array's and printing surface's lateral positional relationship parallel to the microlens array.

41. The printing system of claim 8, further comprising micropositioning transducers disposed around the microlens array's periphery outside of its clear aperture, wherein the transducers apply a controlled force distribution to the array to correct focus and tilt errors and compensate for warp or shape mismatch between the printing surface and microlens array.

42. The printing system of claim 41, further comprising micropositioning transducers which control the microlens array's lateral translational and rotational positions parallel to the microlens array.

43. A method of manufacturing replica microlens arrays comprising the steps of:

first forming a array of low-NA microlenses to be used as a mastering element;

disposing the mastering element above a photosensitive surface, with the surface positioned at the focal plane of the mastering microlenses;

projecting a uniformly-illuminated image field onto the mastering element by means of a projection system which is telecentric at the image side, wherein the projection system's aperture stop contains a transparency mask that is imaged by each mastering microlens onto the photosensitive surface and forms a respective latent exposure image thereon;

scanning the mastering element and photosensitive surface together across the image field as the surface is exposed, while keeping their relative position fixed; and

developing the respective latent exposure images in the photosensitive surface into a microlens array, whereby a replica microlens array is formed with its aperture layout matching the mastering element's aperture layout, and wherein the replica microlenses have identical optical focusing characteristics determined by the aperture mask's transmittance profile.

44. The manufacturing method of claim 43 wherein the mastering element is formed by a photolithographic process in which the mastering microlens positions are defined by an interference pattern, or patterns, between intersecting laser beams which are accurately collimated and uniform over the exposure area, whereby very high positional placement accuracy and high uniformity of the microlenses are achieved.

45. The manufacturing method of claim 43 wherein the mastering microlens array is formed as a surface relief profile in fused silica by a process of laser-assisted chemical etching.

46. The manufacturing method of claim 43 wherein the replica microlens array is formed as a surface relief profile in fused silica by a process of laser-assisted chemical etching.

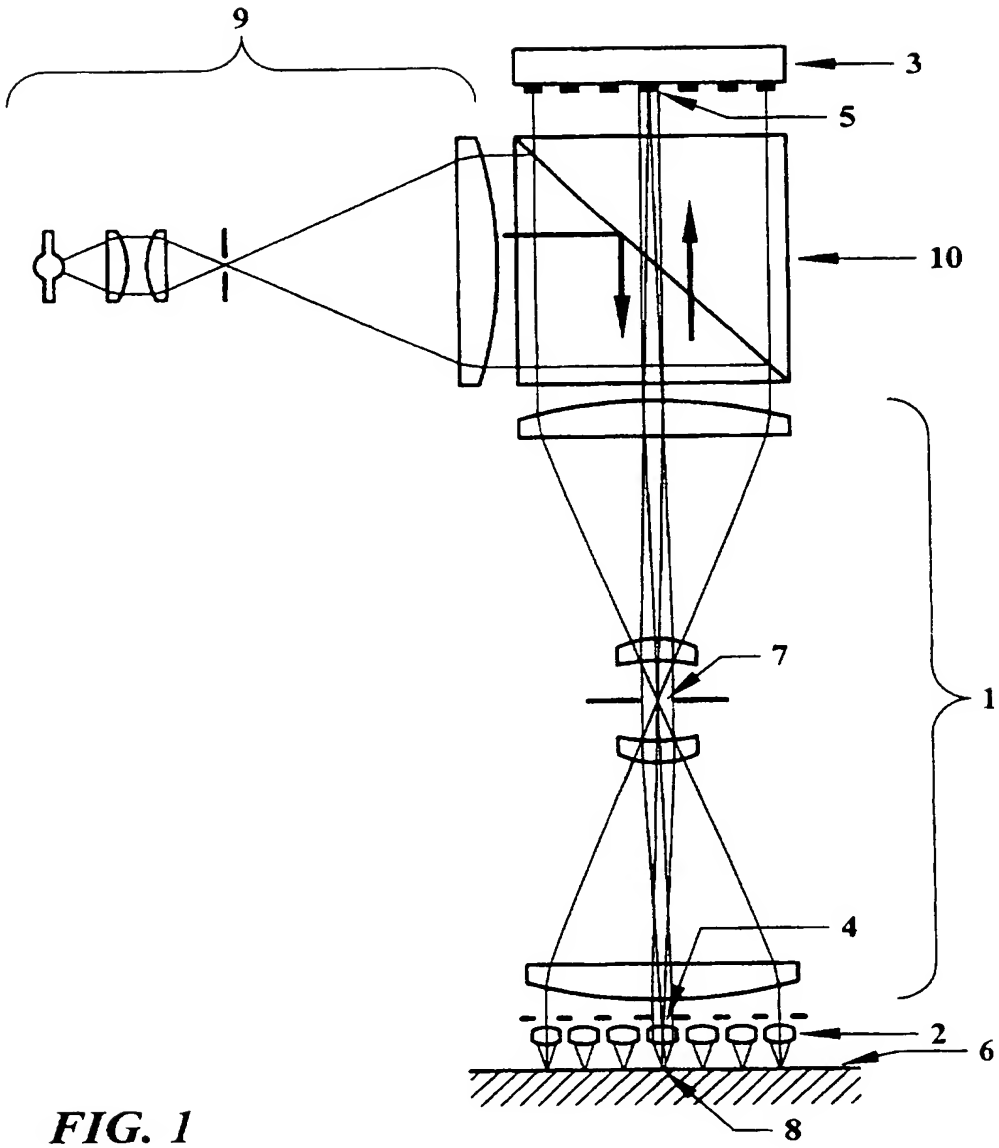

FIG. 1

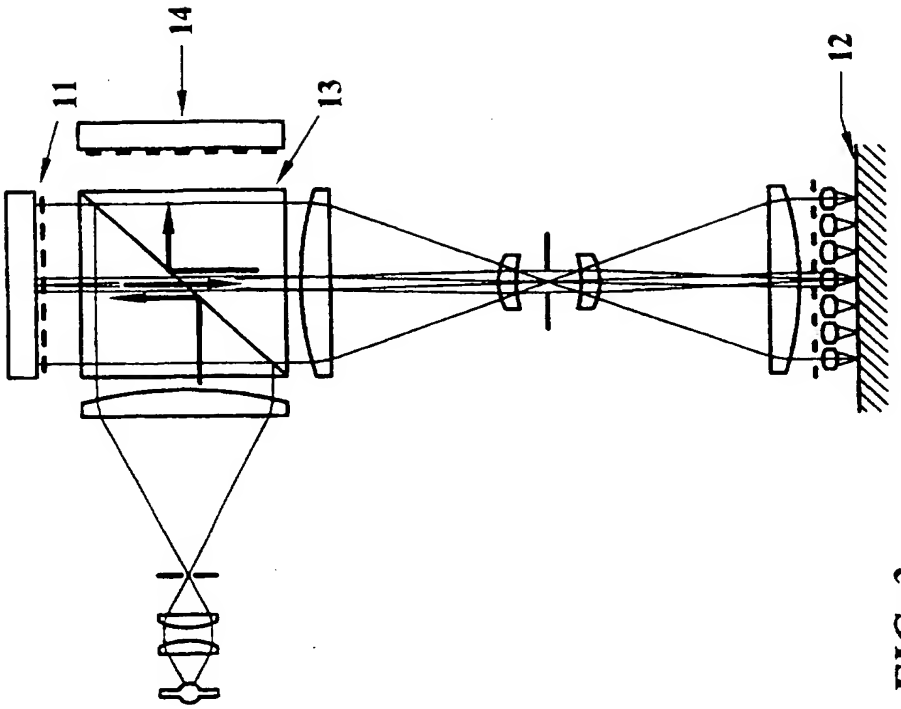

FIG. 3

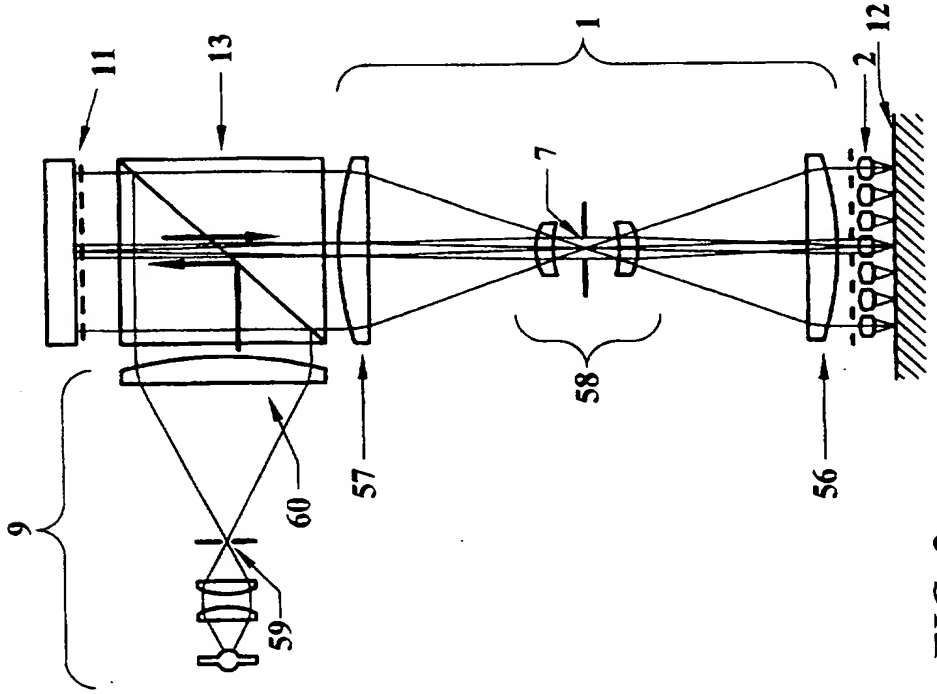

FIG. 2

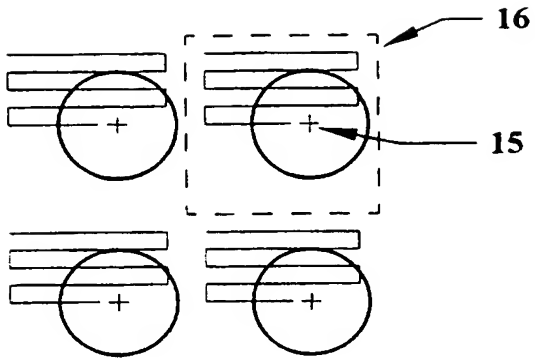

FIG. 4

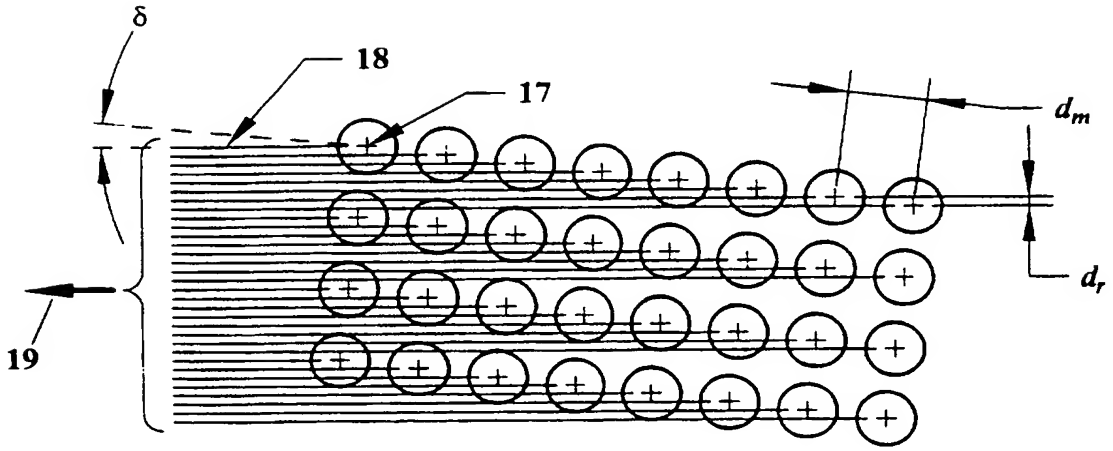

FIG. 5

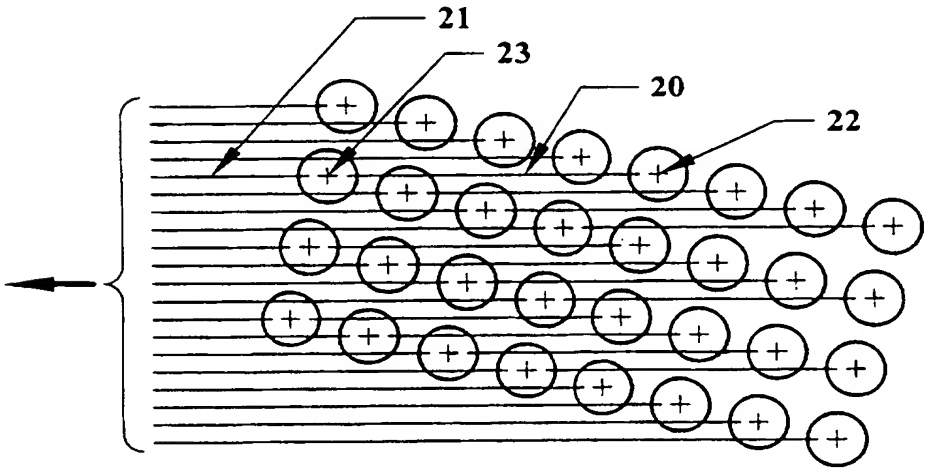

FIG. 6

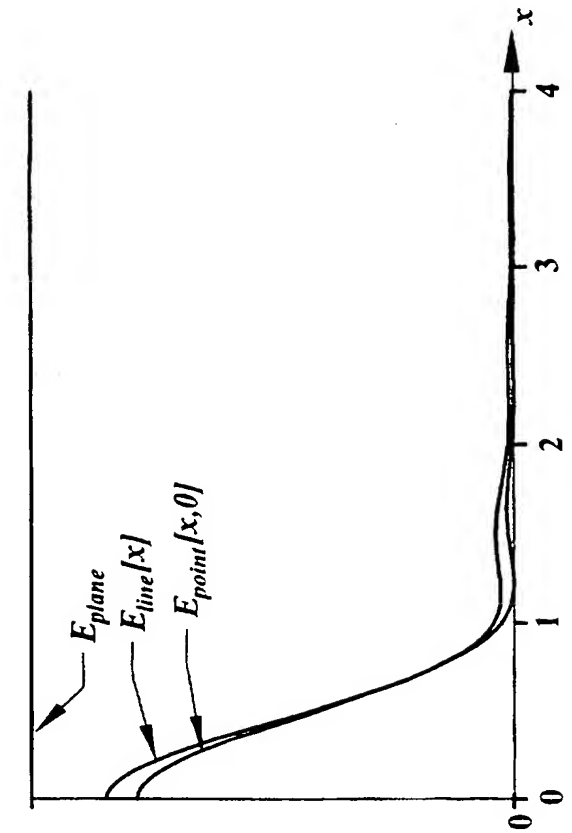

FIG. 8

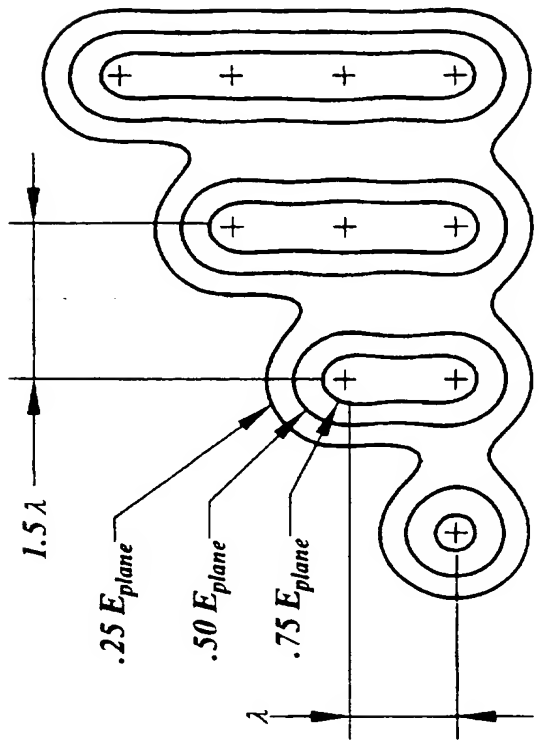

FIG. 10

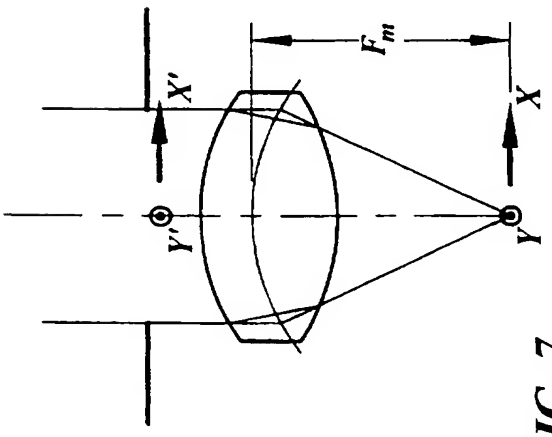

FIG. 7

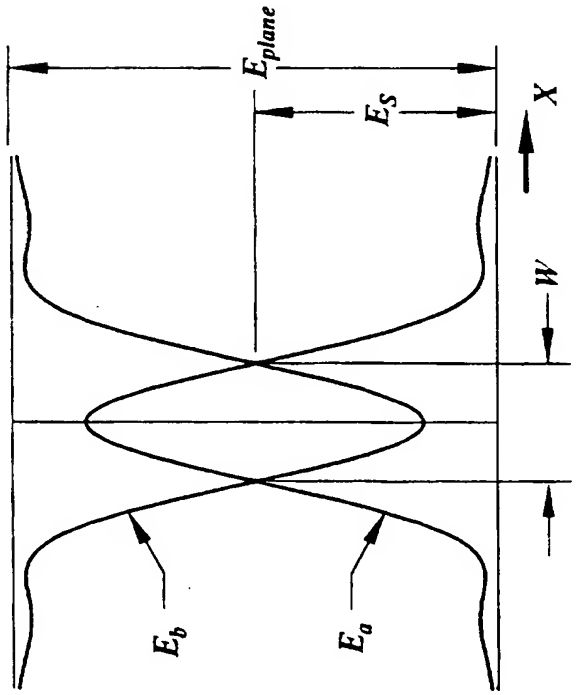

FIG. 9

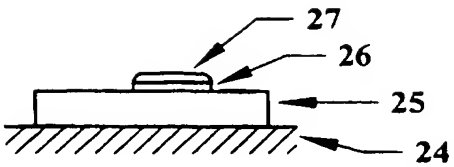

FIG. 11a

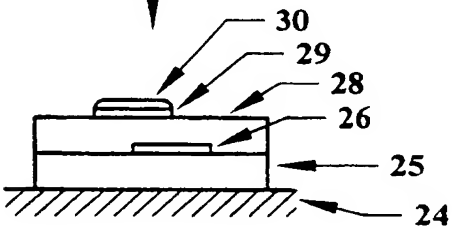

FIG. 11b

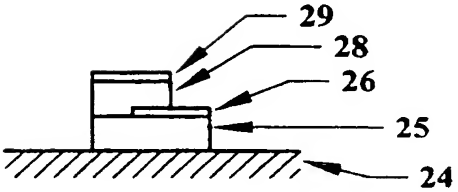

FIG. 11c

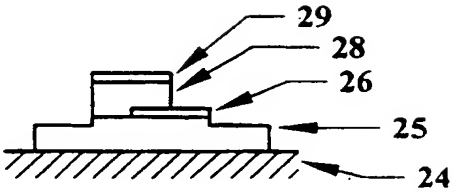

FIG. 11d

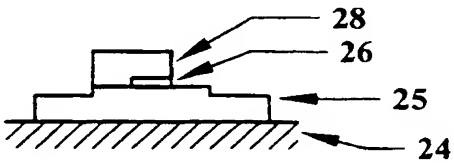

FIG. 11e

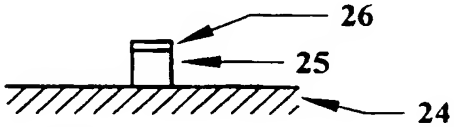

FIG. 11f

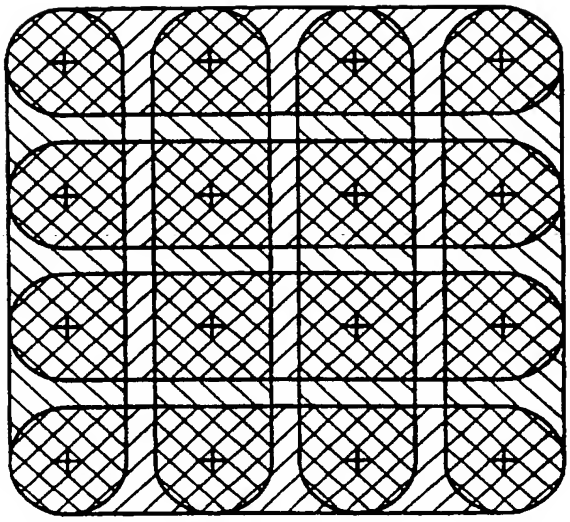

FIG. 12

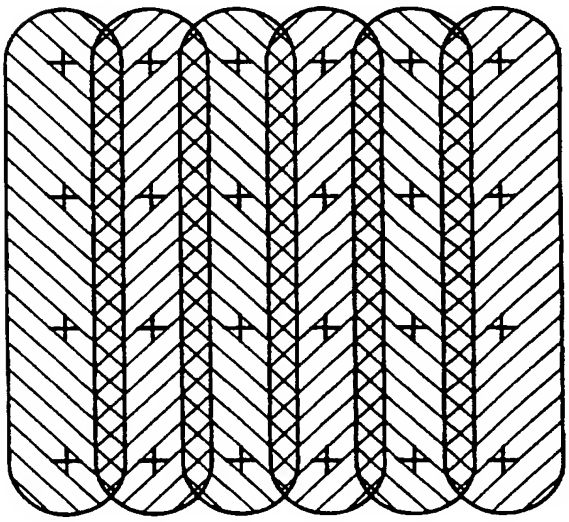

FIG. 13

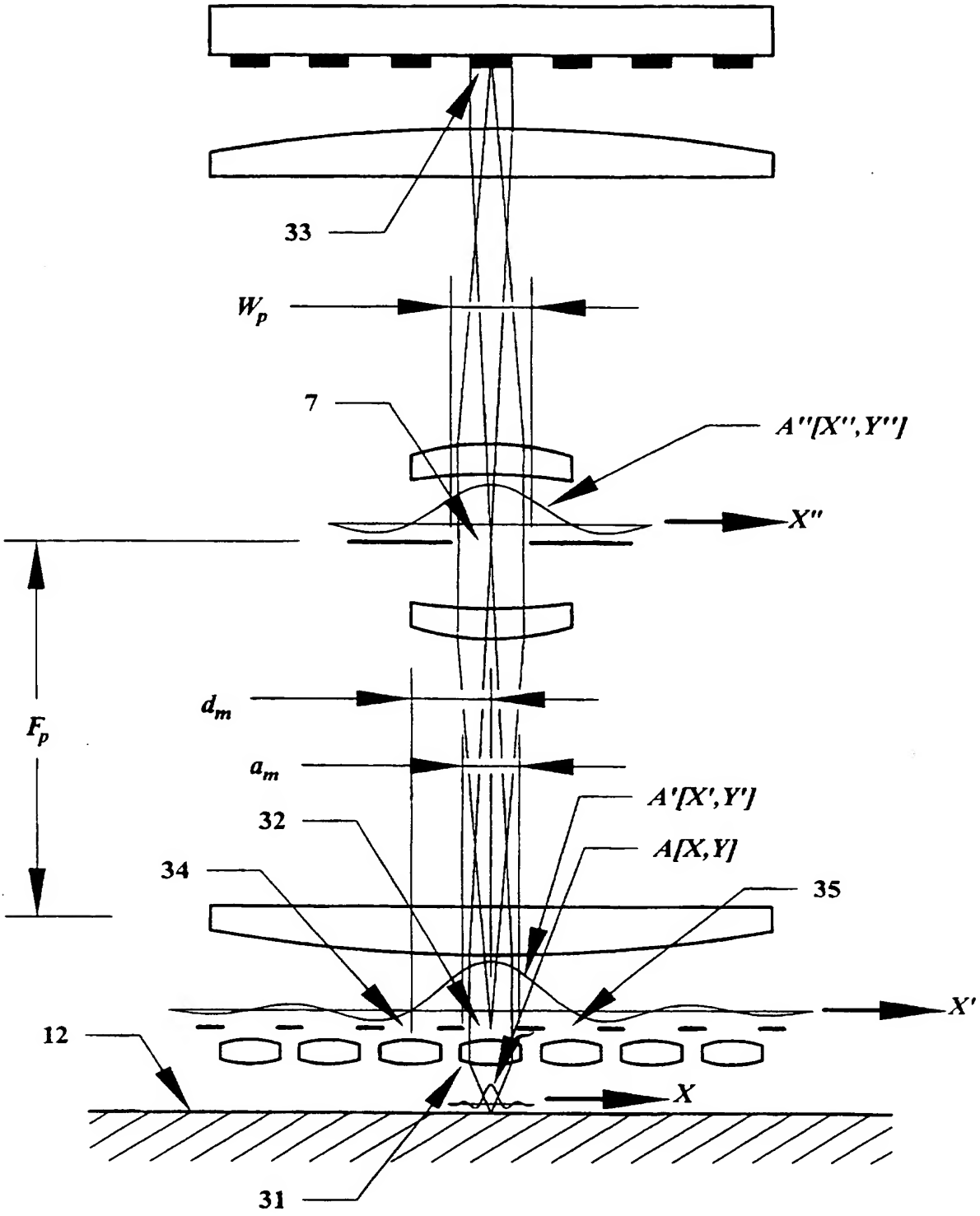

FIG. 14

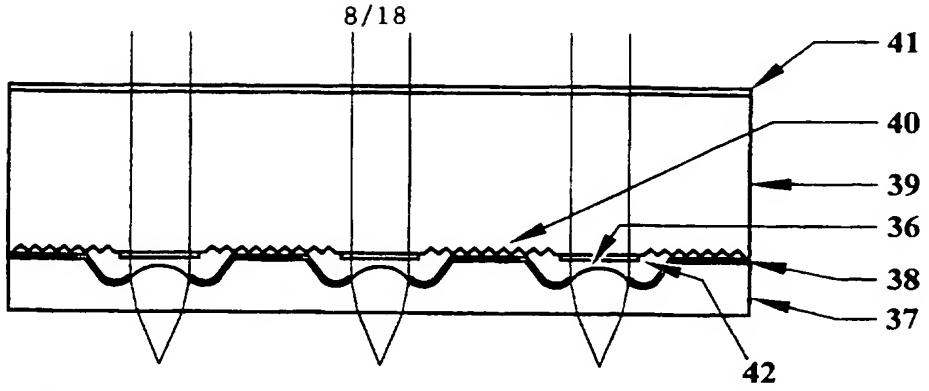

FIG. 15

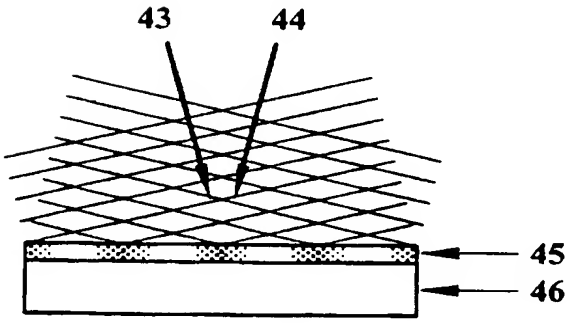

FIG. 16a

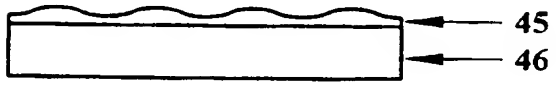

FIG. 16b

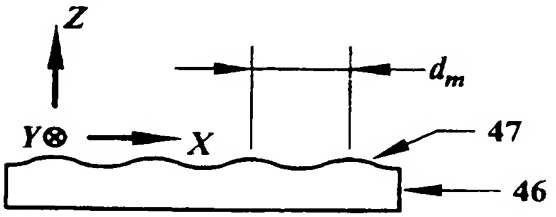

FIG. 16c

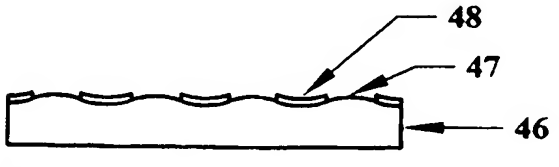

FIG. 16d

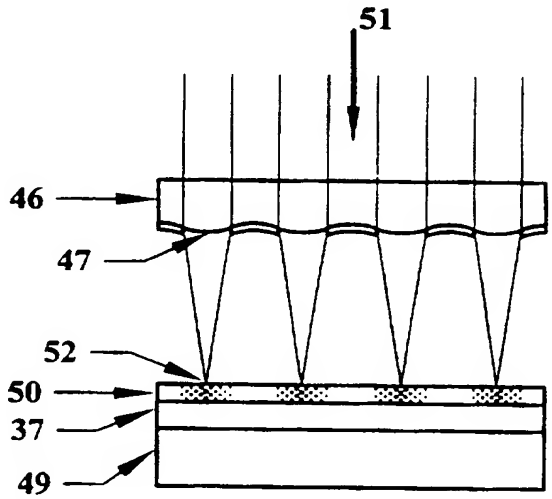

FIG. 16e

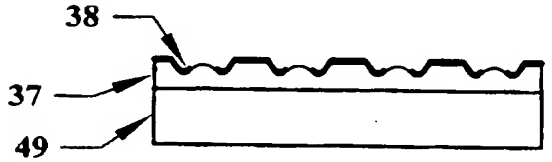

FIG. 16f

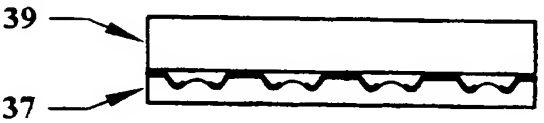

FIG. 16g

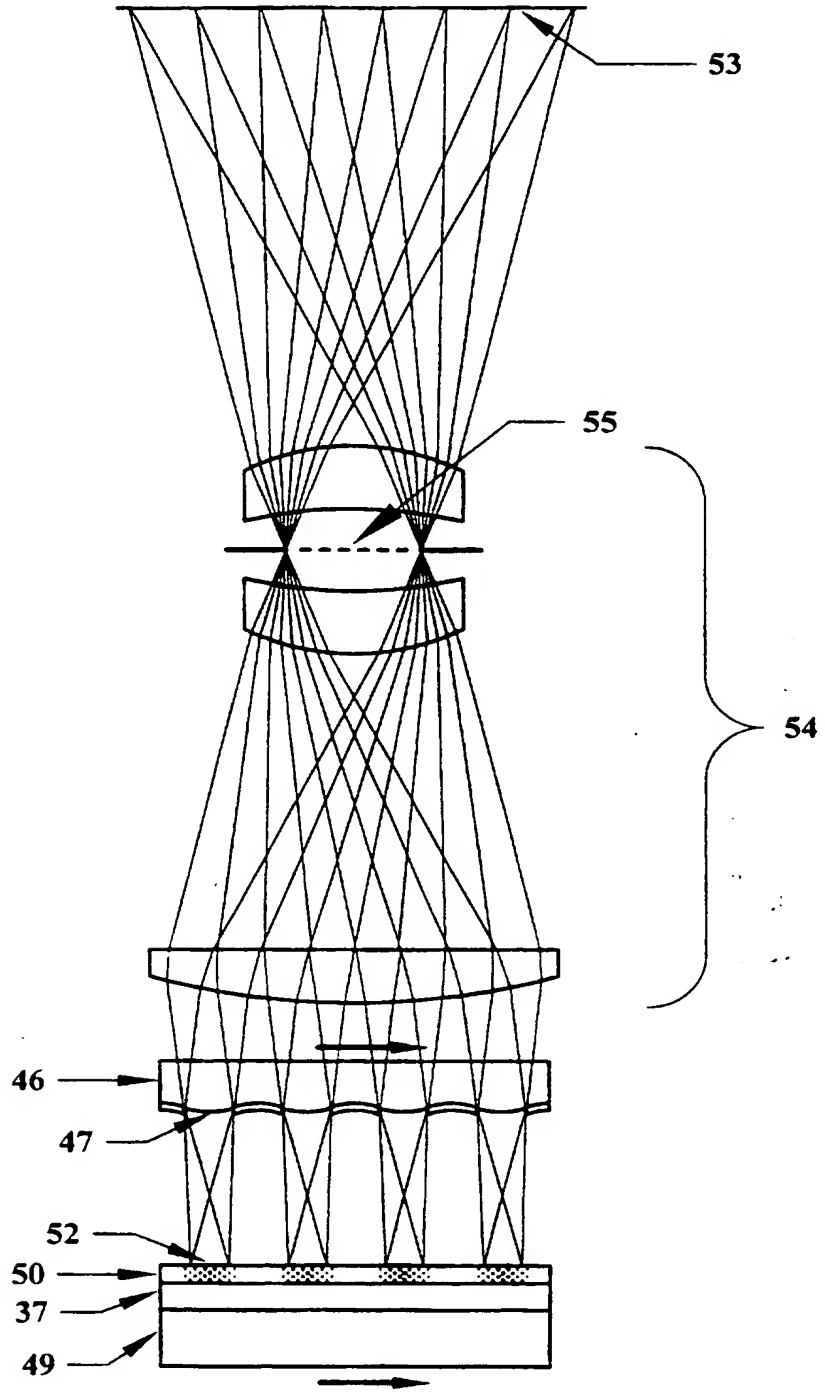

FIG. 17

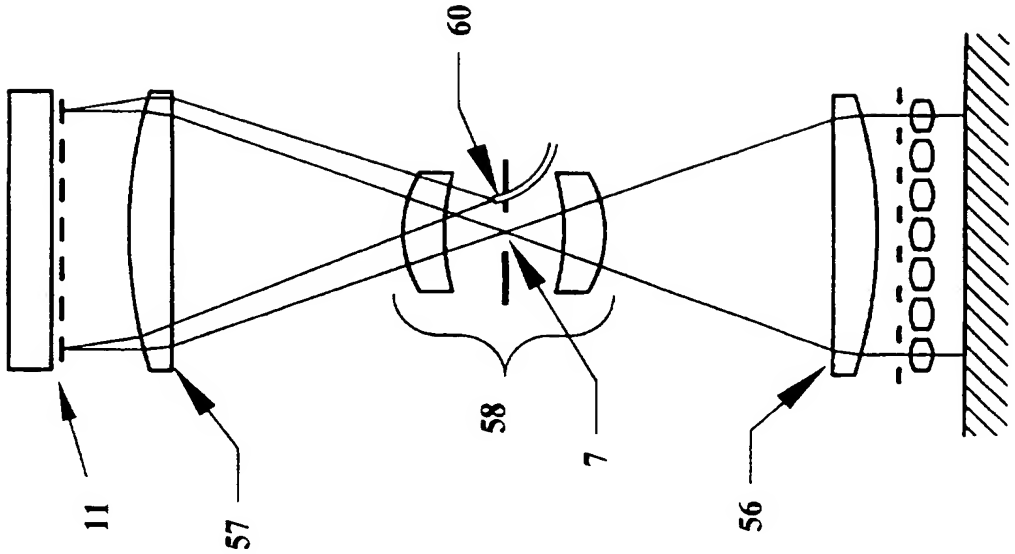

FIG. 19

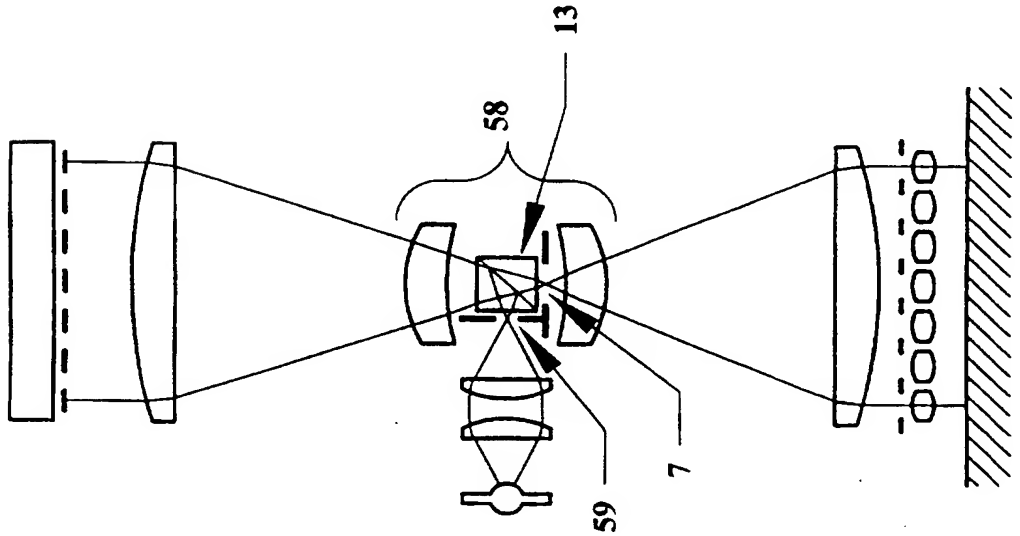

FIG. 18

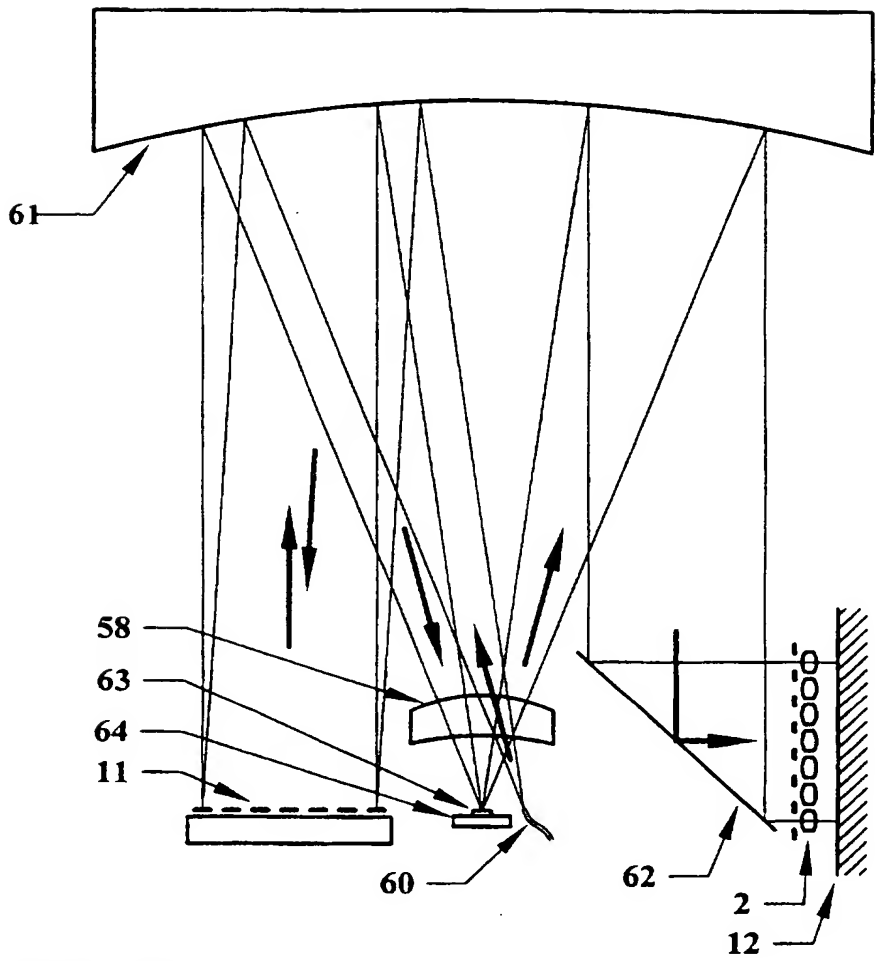

FIG. 20

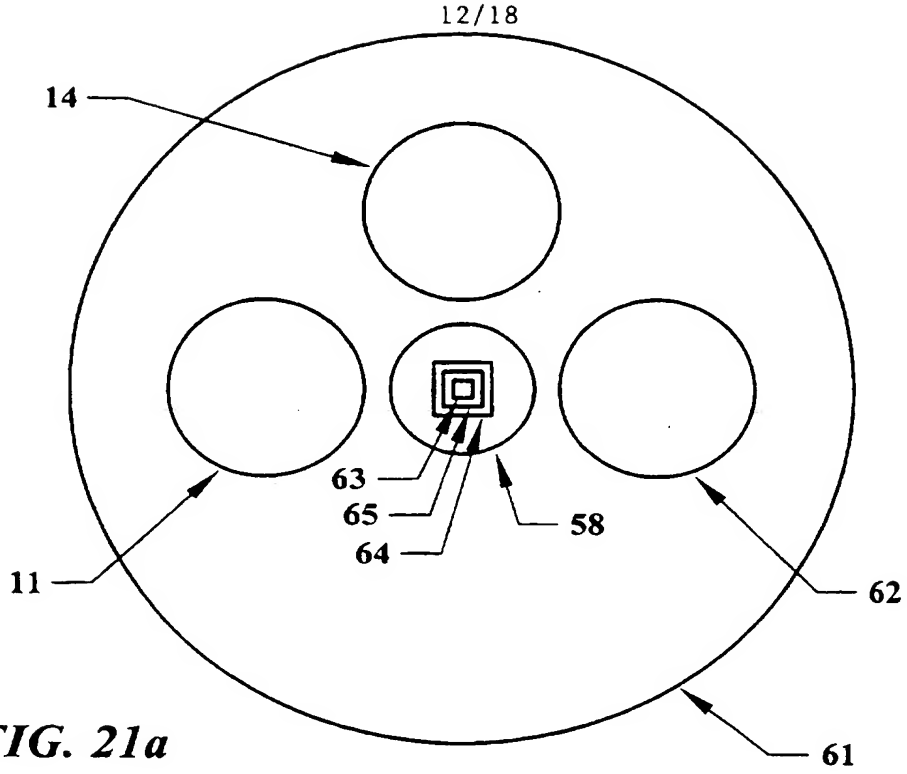

FIG. 21a

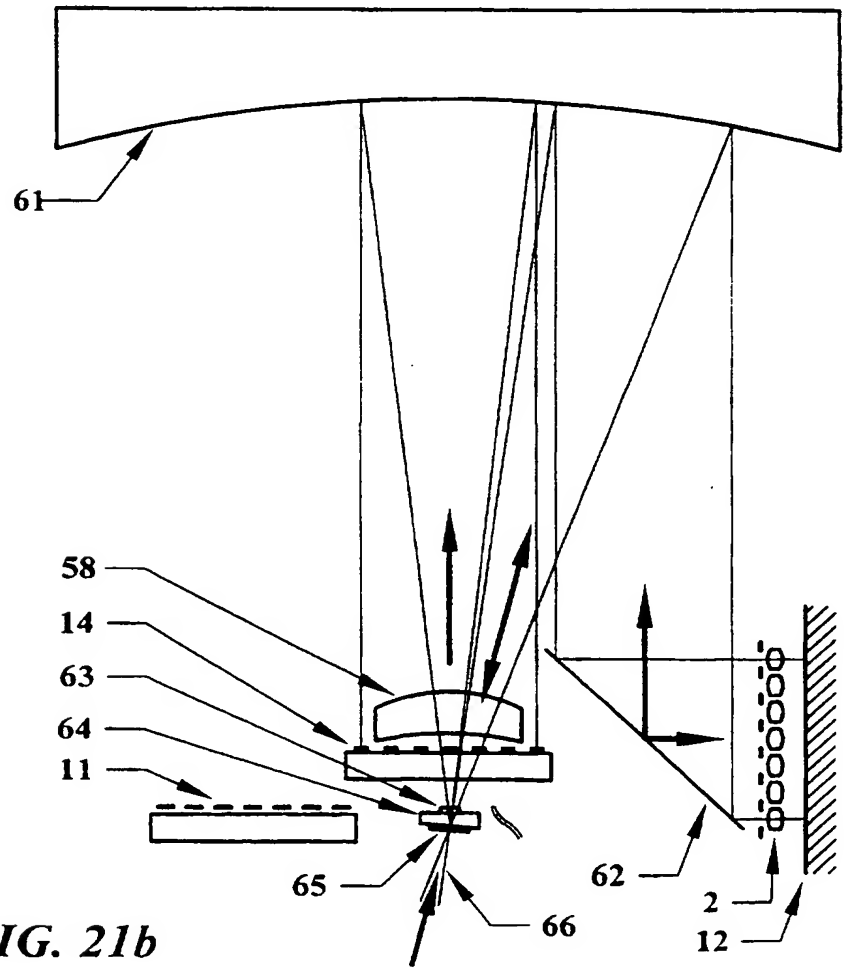

FIG. 21b

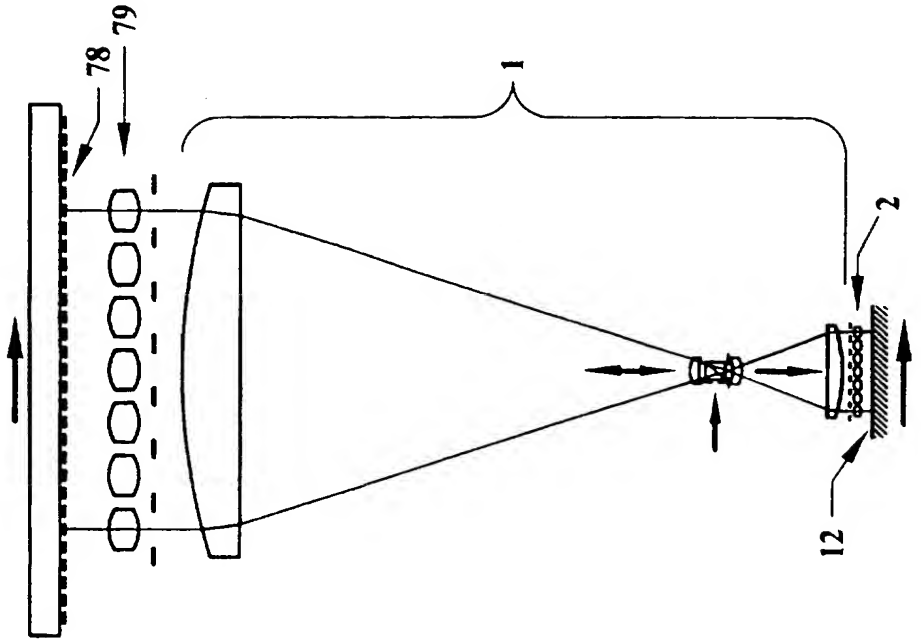

FIG. 23

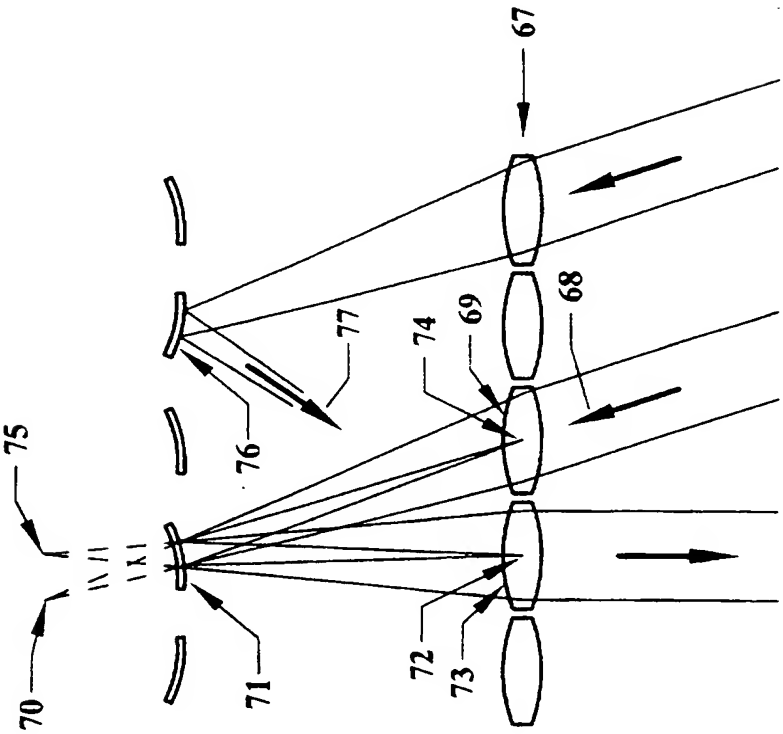

FIG. 22

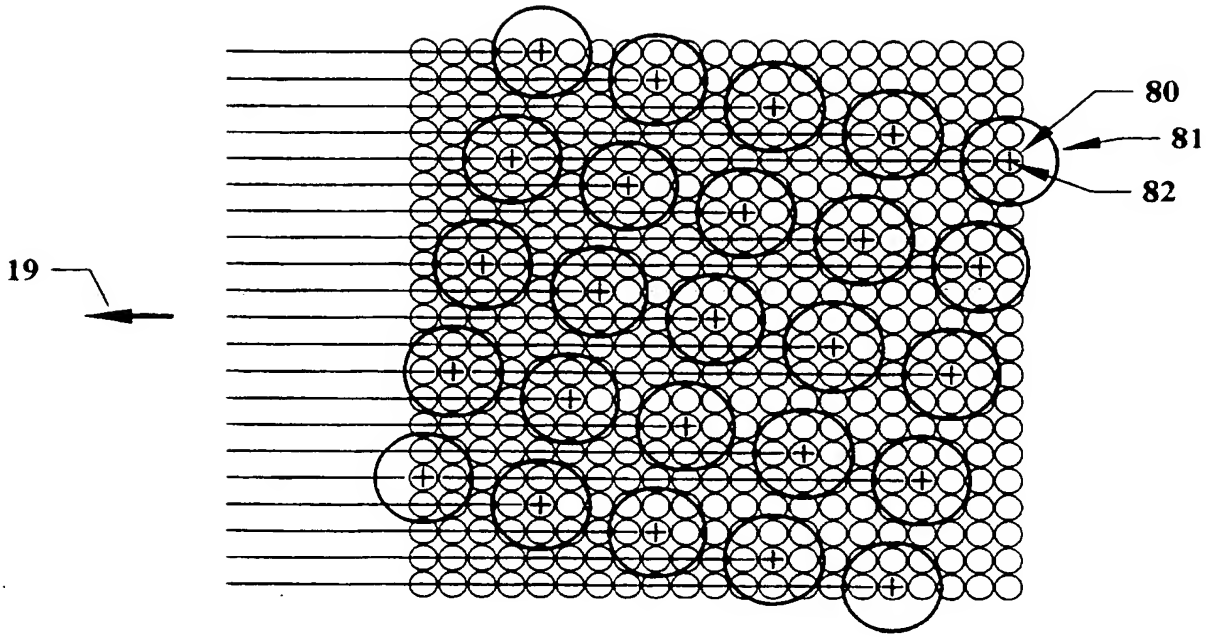

FIG. 24

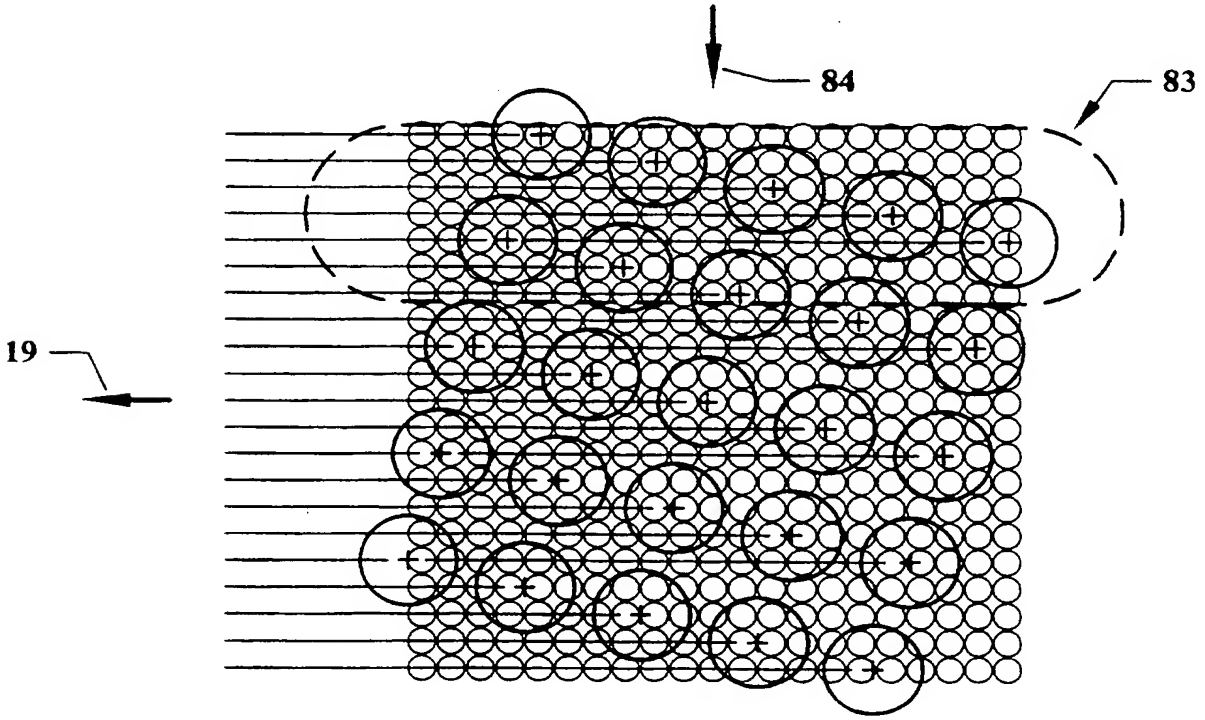

FIG. 25

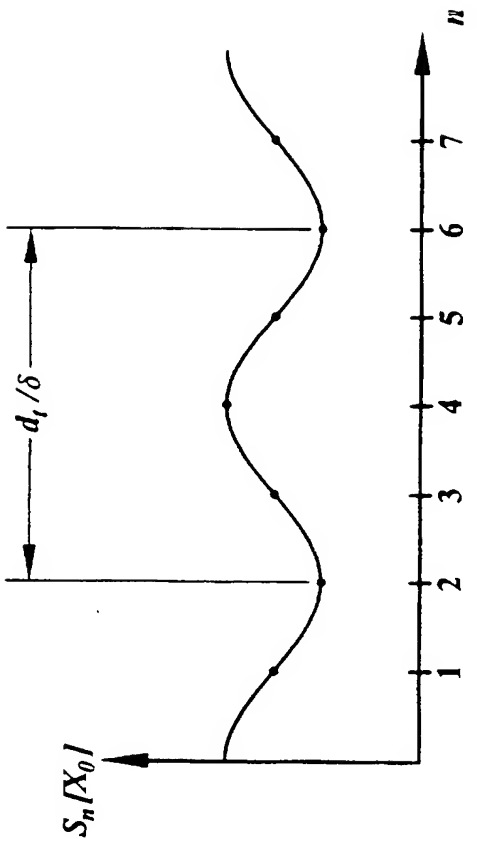

FIG. 27

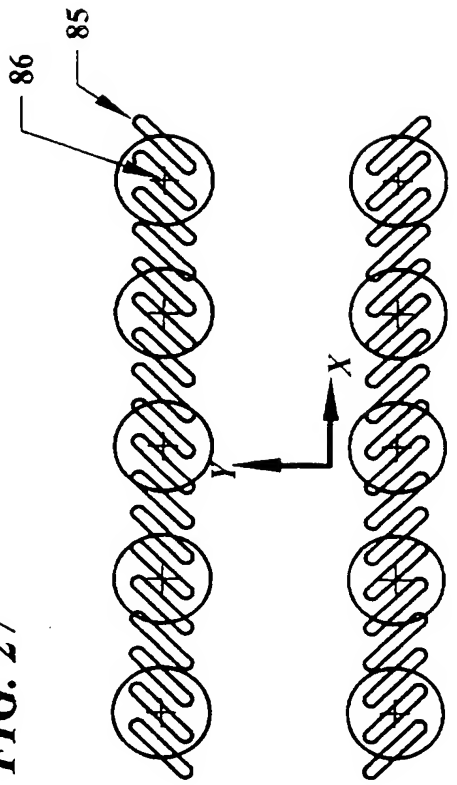

FIG. 29

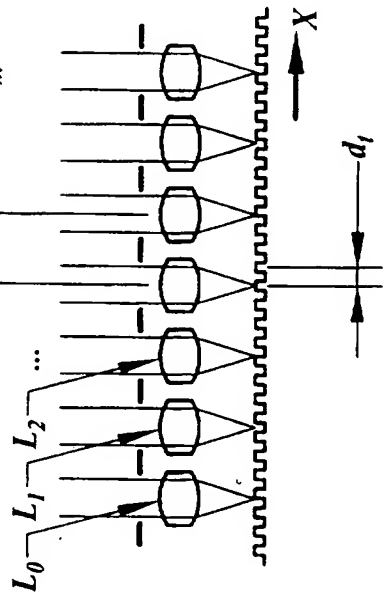

FIG. 26

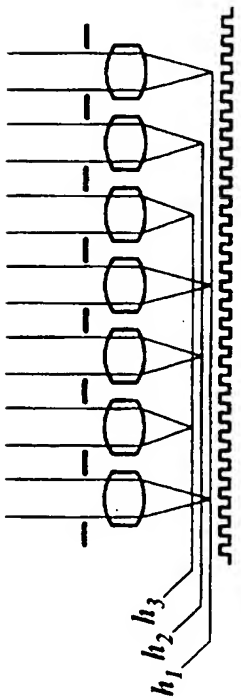

FIG. 28

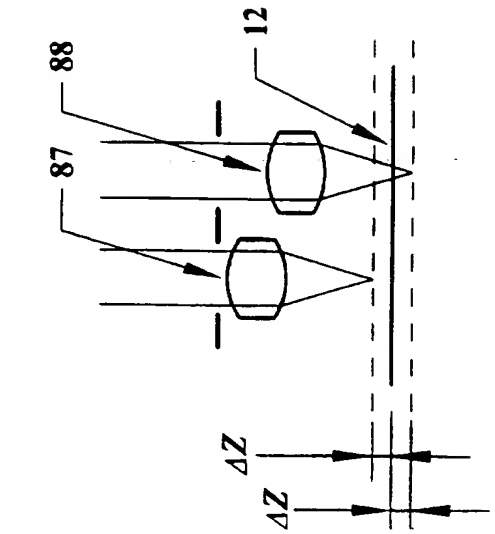

FIG. 31

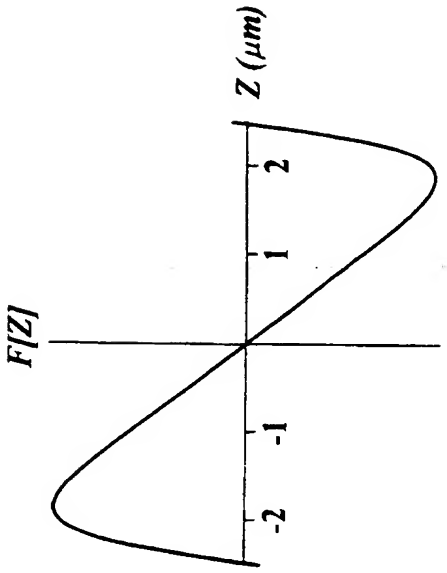

FIG. 33

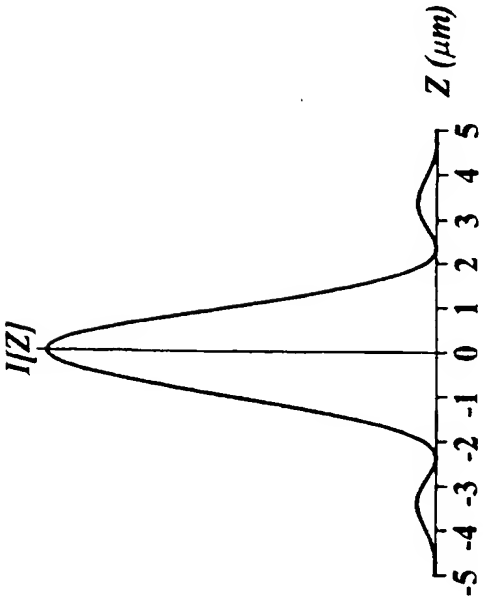

FIG. 30

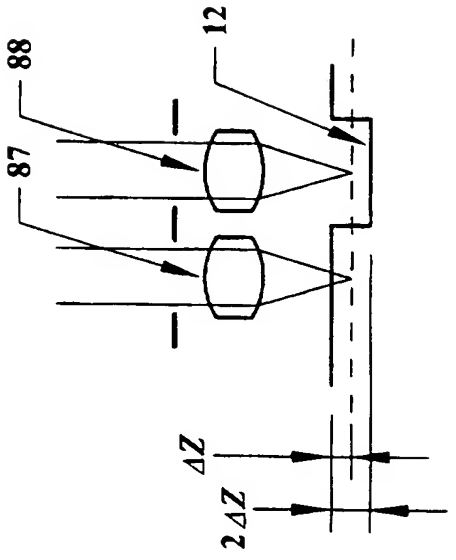

FIG. 32

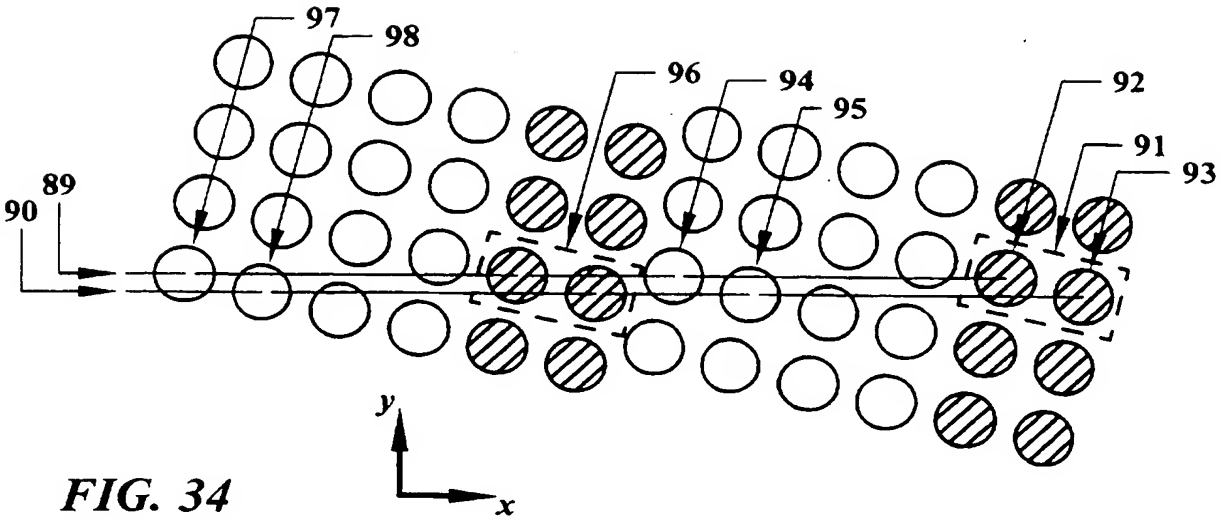

FIG. 34

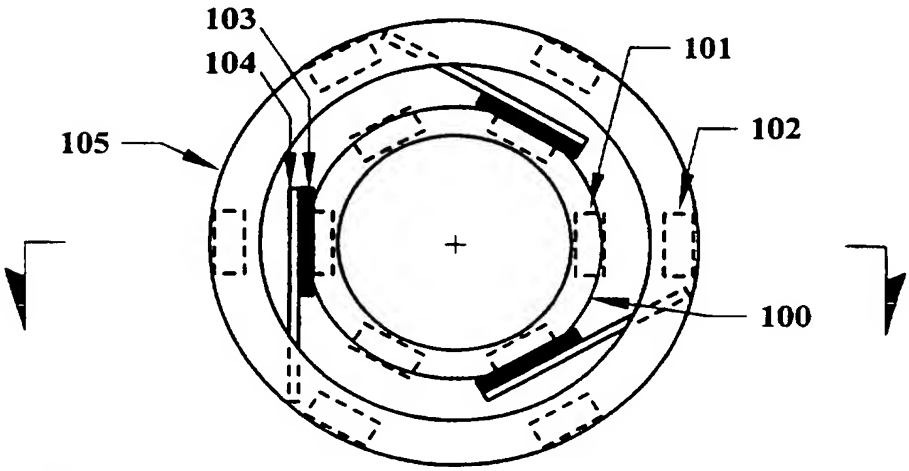

FIG. 35a

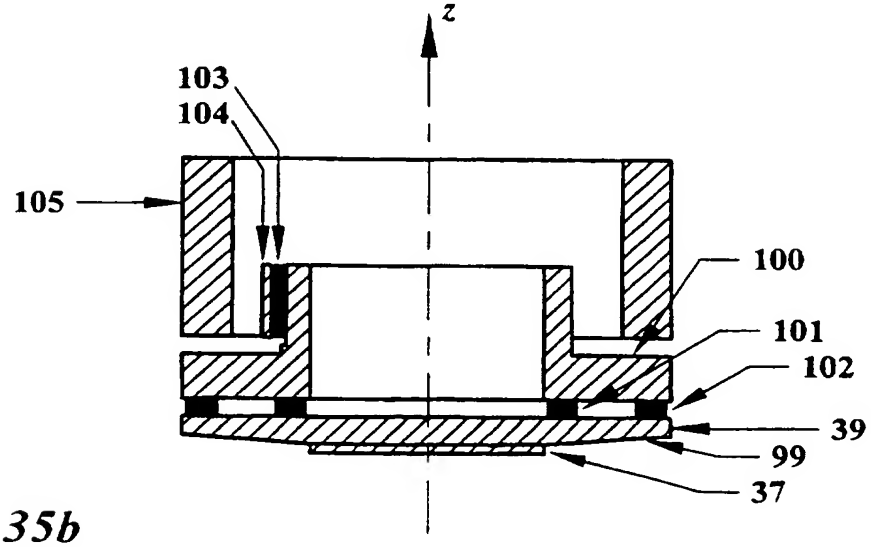

FIG. 35b

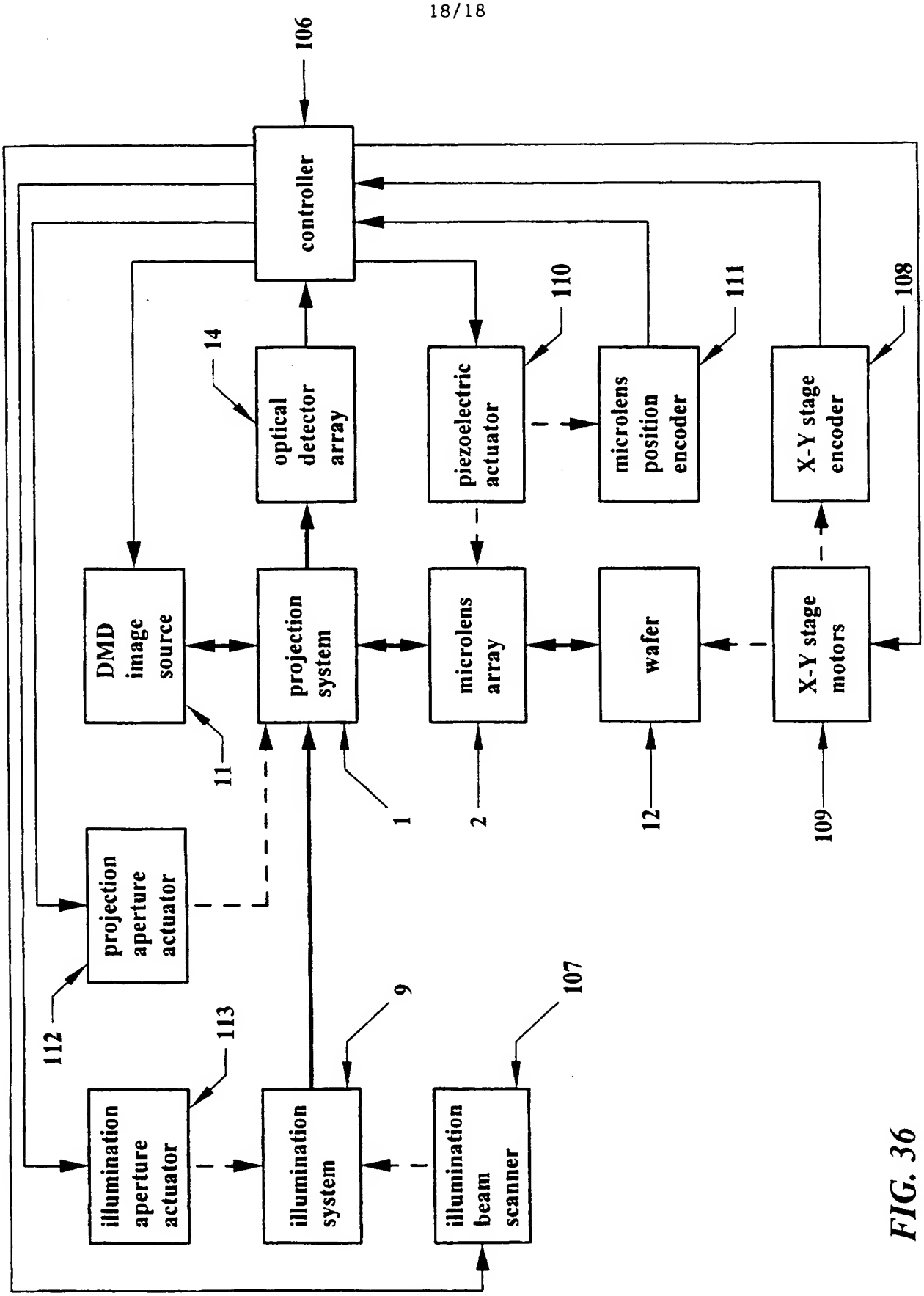

FIG. 36

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(74) Agents: SLONE, David, N. et al.; Townsend and Townsend and Crew L.L.P., 8th floor, Two Embarcadero Center, San Francisco, CA 94111-3834 (US).

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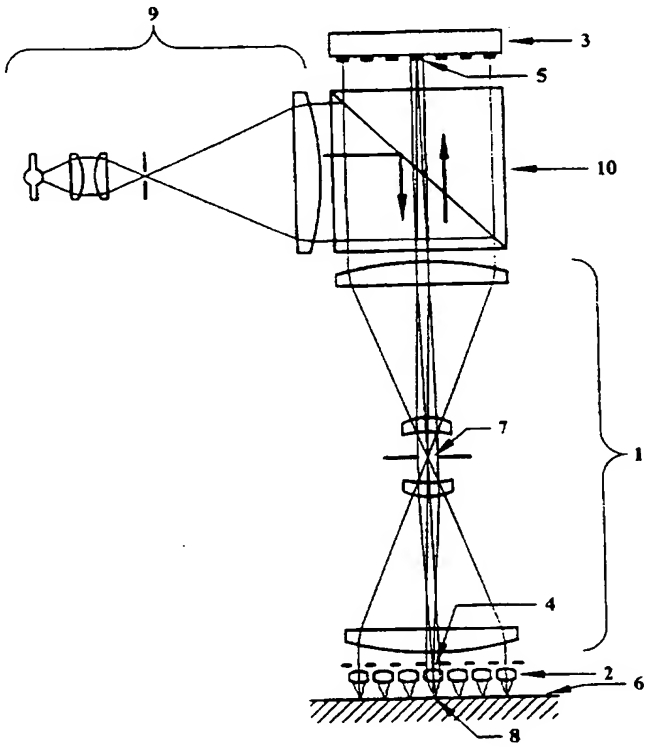
(57) Abstract

A microscopy or lithography system using a low-resolution image projection system, having a very small numerical aperture and large image field, in conjunction with a microlens array (2), each element of which has a large numerical aperture but very small field. The projection system contains a small aperture stop (7) which is imaged by the microlenses (2) onto an array of diffraction-limited microspots on the microscope sample (6) or printing surface (12) at the microlens focal point positions, and the surface is scanned to build up a complete raster image from the focal point array. The system design thus circumvents the tradeoff between image resolution and field size which is the cause of much of the complexity and expense of traditional wide-field, high-NA microscopy and microlithography systems. The system makes possible flat field, distortion-free imaging, with accurate overlay, focus, and warp compensation, over image field larger than the practical limitations of conventional imaging systems. A digital micromirror device may be used as the image source, eliminating the need for photomasks in semiconductor manufacture.



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INTERNATIONAL SEARCH REPORT

International application No.
PCT/US97/02949

A. CLASSIFICATION OF SUBJECT MATTER

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B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 353/ 38, 63, 65, 66, 98, 99, 122; 355/44, 45, 50, 51, 55, 67, 68, 71; 359/368, 369, 372, 385, 389

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US, 5,659,420 E (WAKAI ET AL.) 19 AUGUST 1997 SEE ENTIRE DOCUMENT	1-46
A	US, 5,541,679 P (YANG) 30 JULY 1996 SEE ENTIRE DOCUMENT	1-46
A	US, 5,473,393 A (MANABE) 5 DECEMBER 1995 SEE ENTIRE DOCUMENT	1-46
A	US, 5,245,369 A (UM ET AL.) 14 SEPTEMBER 1993 SEE ENTIRE DOCUMENT	1-46
A	US, 5,225,929 A (ULANOWSKI) 6 JULY 1993 SEE ENTIRE DOCUMENT	1-46

[X] Further documents are listed in the continuation of Box C. [ ] See patent family annex.

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INTERNATIONAL SEARCH REPORT

International application No.
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C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US, 4,668,080 A (GALE ET AL.) 26 MAY 1987 SEE ENTIRE DOCUMENT	1-46
A	US, 4,289,377 A (MATSUI ET AL.) 15 SEPTEMBER 1981 SEE ENTIRE DOCUMENT	1-46

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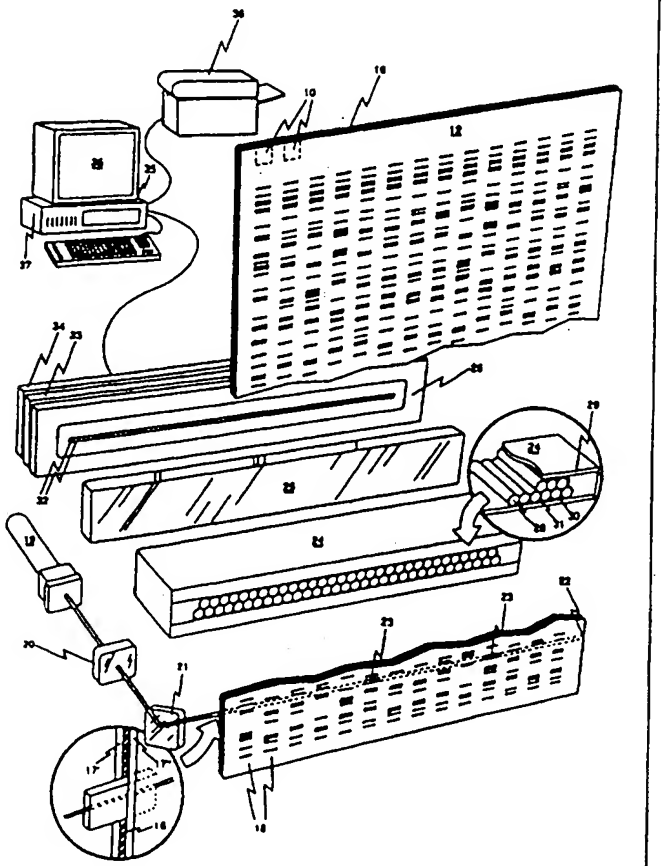
(54) Title: ANALYSIS OF BIOLOGICAL MOLECULES

(57) Abstract

Apparatus (12) and method for detection and separation of biological molecules that are tagged with a photosensitive label. Molecules are separated by size, in both horizontal and vertical planes, in parallel electrophoretic path ways (18) in a gel matrix (16). An electric potential is applied to the gel matrix) while laser light excites the molecules as they migrate in a predetermined direction. The output light signals emitted from the excited molecules are detected, collected, stored and analyzed using a monitor (36), controller (35) and a digital data processor (37).



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ANALYSIS OF BIOLOGICAL MOLECULES

Introduction

Deoxyribonucleic acid (DNA) consists of two linear strands composed of individual nucleosides which are linked to one another by phosphodiester bonds. In its natural state, DNA exists in the form of complementary chains of nucleosides interconnected as a double helix. The double helix is held together by the hydrogen bonds formed between the individual complementary nucleosides situated opposite each other. Nucleotides (composed of a nitrogenous purine or pyrimidine base, a deoxyribose sugar and a phosphate group) are the basic building blocks of the molecule and their sequence defines the gene and ultimately the protein encoded by the gene. There are four nucleotides - deoxyadenosine (A) which pairs with thymidine (T) and deoxyguanosine (G) which pairs with deoxycytidine (C).

The ability to sequence DNA and ribonucleic acid (RNA) has given scientists a valuable tool with which to dissect the genomes of many viruses, bacteria, plants and animals. Indeed, the development of improved and more efficient procedures for the sequence analysis of DNA and RNA has been a crucial element in many of the greatest advances in recombinant DNA technology and genetic engineering.

DNA sequencing technology has now reached the level of sophistication whereby the scientific establishment has been able to undertake perhaps its most ambitious project to date - the DNA sequence analysis of the entire 3,000,000,000 bases of the human genome. Although, in recent years, DNA sequencing technology has seen many advances, both in the protocols used for sequencing reactions themselves and in the means used to visualize the products of these reactions, it is clear that improvements must be made if the task of sequencing the human genome is to be completed within a reasonable length of time and at an affordable cost. The current invention relates generally to an apparatus and methods for the analysis

of labeled biological molecul s. The flexibility and versatility of the current invention allow it to be used in conjunction with a number of different methods of electrophoretic separation, e.g. slab, channel and capillary means. As electrophoretic methods and procedures become more efficient and sensitive, such versatility and flexibility will be of great importance in extending the current invention's utility and viability as a research and diagnostic t ol. Capillary electrophoresis techniques, for example, can be as much as 10,000 times more sensitive than traditional means of electrophoretic detection and be so sensitive as to be able to detect quantities of biological material approaching single molecule quantities.

As detailed below, the invention has particular application to the sequence analysis of DNA and, in this regard, an apparatus for the improved detection and interpretation of the sequence data so derived is described.

BACKGROUND OF THE INVENTION

The determination of the sequence of DNA has been undertaken utilizing two basic approaches: the chemical degradation method of Maxam et.al. (Proceedings of the National Academy of Sciences, Volume 74, pgs. 560-564 (1977)); and the dideoxy chain termination method of Sanger et.al. (Proceedings of the National Academy of Sciences, Volume 74, pgs. 5463-5467 (1977)). The two methods are still widely used, one having advantages over the other depending on specific circumstances. In both the chemical degradation and chain termination methods of sequencing DNA it is necessary to generate labeled DNA fragments, each having a common origin and each terminating with a known base. The labeled-DNA fragments which are a product of either procedure are separated according to size by high resolution gel electrophoresis and a so-called "sequence ladder" is thus generated upon visualization of the gel by exposure to photographic film or other image storage means. Gel electrophoresis usually involves loading the labeled-DNA

fragments onto one nd of a polyacrylamide gel formed between two glass plates in such a way that, at on end, it contains slots or wells for the placement of samples.

During the loading procedure, both ends of the polyacrylamide gel are immersed in an electrolyte solution contained in electrode tanks. When sample loading is completed, a voltage from a power supply is applied across the electrode tanks and thus across the polyacrylamide gel. The applied voltage electrophoreses the labeled-DNA samples through the polyacrylamide gel and so the fragments migrate according to size.

The expense of generating sequence information in terms of both human labor and reagent costs, even when advanced sequencing protocols are combined with the most efficient methods of fragment separation such as those previously discussed, as well as the immense value of such information for research and diagnostic purposes, has led to a number of attempts to make the procedure more efficient. To this end, automation of the methods used for DNA sequencing has proven to be an attractive and often successful proposition. Improvements in the dideoxy chain termination procedure (e.g. Sanger et.al., Journal of Molecular Biology, Volume 143, pgs. 161-178 (1980); Schreier et.al., Journal of Molecular Biology, Volume 129, pgs. 169-172 (1979); Smith et.al., Nucleic Acids Research, Volume 13, pgs. 2399-2412 (1985); Smith et.al., Nature, Volume 321, pgs. 674-679 (1987); Prober et.al., Science, Volume 238, pgs. 336-341 (1987); Church et.al., Science, Volume 240, pgs. 185-188 (1988); and Connell et.al., Biotechniques, Volume 5, pgs. 342-348 (1987)) have made it the method of choice for automated DNA sequencing machines and other rapid sequencing applications.

Manual DNA sequencing procedures and some of the early attempts at automation utilized radiolabeling of fragments i.e. incorporating nucl otides containing a radioactive label such as ^{32}P or ^{3}H into the DNA fragment. For example, U.S. Patent No. 4,707,235 issued to Englert and Wheeler on November

17, 1987 describes a method and apparatus for determining the nucleotide sequence of label d DNA fragments. In the preferred embodiment of the '235 patent, samples containing radioactively-labeled DNA fragments are electrophores d through a gel matrix. As the labeled fragments migrate to th bottom of the gel, they pass the window of a detector. Ionizing radiation from the radiolabeled fragments of sufficient energy passes through the window, producing free electrons in the gaseous environment of the detector. The free electrons are accelerated towards an anode wire which, in response, produces electronic signals. The electronic signals so generated are ultimately stored and interpreted by means of a computer.

However, as the availability and efficiency of fluorescent-labeling techniques improved, detection of DNA sequence information by fluorescence became the method of choice, especially in fully automated systems. Excitation of fluorophore-labeled DNA fragments during electrophoresis through a gel matrix combined with fluorescence detection systems and computer-based methods of data interpretation and storage have allowed the generation of sequence information in an increasingly more labor efficient and cost effective manner.

A variety of strategies can be utilized in order to derive DNA sequence data using DNA fragments labeled with fluorescent dyes e.g. using only one fluorescent dye, and sequence information obtained from a parallel analysis of four lanes on a gel (Ansorge et.al., Journal of Biochem. Biophys. Methods, Volume 13, pgs. 315-323 (1986); Ansorge et.al., Electrophoresis, Volume 13, pgs. 616-619 (1992)); using four dyes, each associated with a specific base, and the sequence information obtained from analysis of one lane on the gel (Smith et.al. Nature Volume 321, pgs. 674-679 (1986); with the use of different dyes, T7 DNA polymerase, manganese, and inorganic pyrophosphatases in c mbination with an analysis of peak heights (see U.S. Patent No. 5,124,247 issued to Wilhelm

Ansorge on June 23, 1992; Tabor and Richardson, Journal of Biological Chemistry, Volume 265, pgs. 8322-8329 (1990)); or with the use of different dyes in combination with a two-laser-two-window automated approach for maximum signal and dye discrimination (Carson et.al., Analytical Chemistry, Volume 85, pgs. 3219-3226 (1993)).

In the majority of systems utilizing fluorescent labeling techniques, the fluorescent dyes are attached either to a primer, e.g. Smith et.al. (1987, cited above); the base of a terminal dideoxynucleotide, e.g. Prober et.al. (1987, cited above); or to internal nucleotides of the DNA fragment (see PCT Application WO 93/03180, Wilhelm Ansorge and Hartmut Voss).

The latter method of labeling utilizes labeled deoxynucleoside triphosphates e.g. deoxyadenosine triphosphate (dATP), and is particularly advantageous in that it allows the use of unlabeled primer. When combined with optimal primer design, fragment labeling with fluorescent dATP enables sequence information to be read beyond 1000 bases from a single lane or group of four lanes after electrophoresis of the labeled DNA fragments through a gel matrix. The increased amount of sequence data that can be obtained from a single gel is due, in part, to the increased efficiency of DNA fragment labeling disclosed in the Ansorge and Voss protocol.

No matter the labeling procedure, the labeled fragments, as discussed above, are loaded onto a gel for electrophoretic separation and the DNA sequence is determined from the pattern of fluorescent signals emitted by the fragments as they pass a detector during the separation process.

Critical components of automated DNA sequencing machines are the optical systems used to collect and focus fluorescent light onto the fluorescence detection system and the fluorescence detection systems themselves. Numerous approach s have been taken in the design of these components. With regard to the fluorescence detection systems, two types have shown considerable utility in automated DNA sequencing

machines - thos which use CCDs and those which use diode/amplifier assemblies as th primary means of fluorescence detection.

Linear CCDs in the CCD-based fluorescence detectors are divided into a vast number of photosensitive cells, often as many as 5,000. Two-dimensional CCDs, which can also be utilized in the CCD-based fluorescence detectors, contain even more such photosensitive cells. Information from the cells can be analyzed on an individual or collective basis. This ability imparts a high data collection sensitivity and efficiency to the detection system. The sensitivity of the CCD-based detector systems is increased when they are combined with optical systems which can efficiently capture the fluorescent light emitted by excited fluorophore-labeled DNA fragments as they migrate through the matrix of a gel.

Although diode/amplifier-based detection systems have been incorporated into the design of a number of automated DNA sequencing systems, their utility has been limited by physical constraints. In such DNA sequencing machines, each lane on the gel must correspond to a discrete diode which is separately combined with a signal amplifier. In the discrete diode/amplifier detection systems, any increase in the number of lanes on the gel must be accompanied by a concomitant increase in the number of diodes. Recent innovations such as those which have allowed the integration of multiple amplifiers and diodes into a single unit have enabled diode/amplifier-array-based fluorescence detection systems to overcome some of the disadvantages associated with their use. As with the CCD-based detection systems, the sensitivity of the integrated diode/amplifier-array-based fluorescent detection systems can also be increased when they are combined with optical systems which can efficiently capture fluorescent light emitted by excited fluorophore-labeled DNA fragments as they migrate through the matrix of the gel.

AUTOMATED DNA SEQUENCING MACHINES

At present, the commercially available automated DNA sequencing machines can be divided into two types - those which use a scanning laser means to excite fluorescence and those which use fixed laser means to achieve this goal.

Scanning Fluorescence Detection

DNA sequencing machines which rely on a scanning laser excitation means are exemplified by the apparatus described in U.S. Patent No. 4,811,218 issued to Hunkapillar et.al. on March 7, 1989.

The '218 patent describes an automated DNA sequencing apparatus which uses a laser as the source of the fluorescence-inducing electromagnetic radiation. An optical excitation system which moves horizontally on a motorized translational stage consists essentially of a focusing telescope which decreases the size of the incoming laser beam and then focuses it onto each of the gel lanes, independent of one another. A collector lens system collects a portion of the fluorescence from the labeled DNA fragments on the gel and directs it toward a filter wheel made up of four filters. Located at the focus of the collector lens is a Fabry lens group, configured so as to image the collected light onto the active area of a photomultiplier tube. The photomultiplier tube generates a signal which can be interpreted by appropriate means and converted to readable DNA sequence information.

Light from the laser is launched into the gel lanes at the Brewster angle. This detection means calls for utilization of a laser of high power. The use of the high power laser for the purposes of illumination is expensive and results in a higher cost for the apparatus.

Another significant disadvantage of the apparatus described in the '218 patent involves the integration time for the information contained in the lanes of the gel which are scanned. A band on a gel containing a labeled fragment is examined for a shorter time in a laser scanning excitation

system than in a static laser excitation system. This shorter scanning time results in a shorter detector integration time because the laser must not only scan each lane but also scan at different emission wavelengths to collect sufficient data points in order to make a base determination. In addition, the use of mechanical means for scanning causes a reduction in the system's overall reliability.

DNA sequencing machines utilizing the laser scanning means of excitation are marketed by Applied Biosystems Inc. of Foster City, California and Li-cor, Inc. of Lincoln, Nebraska. The Li-cor apparatus uses an infra-red dye, an avalanche diode and a mass produced semiconductor laser instead of the expensive Argon laser. Although these improvements have reduced the cost of the apparatus, they have not resulted in the amelioration of all of the disadvantages inherent in the laser scanning detection machines.

Fixed Fluorescence Detection

The fixed detection system used in DNA sequencing machines is exemplified by the automated apparatus described by Ansorge et.al. (1986), cited above; and Ansorge et.al., FRG Patent Application Nr. P36.18.605.B (1986). This apparatus consists of a laser, light from which passes through the entire width of a gel, inducing fluorescence from fluorophore-labeled DNA fragments migrating within the gel matrix, and a system for detecting and monitoring the emission of fluorescence from all four lanes.

U.S. Patent No. 4,675,095 issued to Kambara et.al. on 23 June, 1987 describes an automated DNA sequencing apparatus consisting of a laser as a source of fluorescence-inducing electromagnetic radiation, a fluorescence detection system and a computerized data storage and interpretation system. In the apparatus of the '095 patent, the light from the laser is launched horizontally into the gel from the side, i.e. in a direction which is perpendicular to the migration of the DNA bands.

The apparatus described in U.S. Patent No. 5,294,323 issued to Togusari et.al. on 15 March, 1994 also uses a laser, light from which is launched horizontally into the gel from the side as described in the '095 patent, as a means of fluorescence-inducing electromagnetic radiation. Fluorescence from the DNA bands is reflected by means of mirrors into a multi-component fluorescence detector. The fluorescence detector consists of an imaging lens; a bandpass filter attached to the distal end of the imaging lens; a solid state imaging device such as a photodiode, CCD sensor or MOS linear image sensor in alignment with the optical axis of the imaging lens; and a Peltier device which provides cooling to the solid state imaging device.

In one embodiment of the '323 patent, the fluorescence detected from each lane on the gel is condensed onto an image intensifier. The amplified image is converted to an electrical signal by a photodiode array. The electrical signal produced in this manner is processed with the aid of a computer into readable DNA sequence data.

The manner described by the '095 and '323 patents for launching light from the laser into the gel allows DNA sequence information to be generated using a low power laser. This therefore offers a significant cost saving in the manufacture of the machine. In addition, the use of a static laser excitation system, as alluded to above, results in a higher accuracy at faster separation speeds.

However, the apparatus of the '323 patent is deficient in that there is low light collection efficiency from the fluorescence of the DNA bands. In the embodiment of the '323 patent which utilizes the CCD detector, for example, this arises because there is a large disparity between the size of the gel being imaged and the size of the CCD used in the detector. The lens required to demagnify the image of the gel onto the CCD leads to a low efficiency of fluorescent light collection (the detector/lens combination "sees" a small solid angle). As a consequence of this detector design, signal

level is compromised. Due to the compromised signal level the dynamic range and sensitivity of the detector is limited. In order to overcome the limitations of the detector, more expensive scientific grade CCDs (when compared to widely used commercially available CCDs) must be utilized or more stringent approaches to noise reduction must be taken, e.g. detector cooling or lower noise CCDs.

The apparatus described in U.S. Patent No. 5,307,148 issued to Kambara et.al. on April 26, 1994 uses laser illumination from the side of the gel in the same way as the apparatus of the '095 and '323 patents. Unlike the '323 patent however, the '148 patent describes the use of multiple lasers which are placed parallel to one another and launched from the side with their beams spaced apart by at least one centimeter. In the preferred embodiment, the apparatus utilizes two lasers. The two laser beams are first spectrally dispersed, filtered and then refocused to form eight spectrally distinct line images (four from each laser line) on a two dimensional CCD detector. This arrangement allows use of multiple dye labels in one lane of the electrophoresis gel and allows for the respective signals to be recovered from the different emission and excitation spectra.

However, the apparatus of the '148 patent is deficient in a number of respects. The arrangement of lenses and detector, for example, is not an improvement over the apparatus of the '323 patent in terms of detector sensitivity. The sensitivity of the detector is not improved because the light collection angle is limited by the collection optics in that the optics utilize an image reduction two dimensional CCD detector. Furthermore, the apparatus of the '148 patent is deficient in that the information derived from the two laser lines is displaced in time because of the spatial separation of the beams; the launch conditions for the two lasers in unnecessarily complicated; and the collection optics are overly complex in addition to being inefficient.

SUMMARY F THE INVENTION

It is an object of the present invention to provide, in a simple, cost effective manner, an apparatus for the analysis of biological molecules which is capable of high horizontal and vertical resolution. Although the discussion is presented in terms of electrophoresis performed in the vertical plane, it should be remembered that the following applies equally to electrophoresis performed in the horizontal plane. Furthermore, for reasons of clarity, and because of the importance of the application, the discussion is presented in terms of DNA sequence determination. This presentation should in no way be interpreted to limit the scope of the present invention. The present invention has equally valuabl potential application to the analysis of other types of biological molecule, e.g. determination of RNA sequence data, as well as to techniques involving or related to sequence data, e.g. mapping and fingerprinting techniques. In addition, the present invention can be used with a variety of other photon emitting detection techniques in addition to fluorescent labeling.

The apparatus of the present invention achieves its objective in a simple yet elegant and cost-effective manner by the use of affordable, commonly available, mass manufactured optical components to focus the fluorescent light emitted by excited fluorophore-labeled DNA fragments onto a fluorescence detection system. Although the apparatus of the present invention is described in combination with CCD and diode/amplifier-based fluorescence detection systems, it is envisaged that it can be effectively used in combination with any design of fluorescence detection system.

As mentioned previously in the discussion of CCD and diode/amplifier-based fluorescence detection systems, increased horizontal resolution can be attained in DNA sequencing machines by combining the fluorescence detection syst m with higher efficiency optical systems which will focus more light onto the detector. Use of an array of gradient

index (GRIN) lenses such as the SELFOC lens array (SLA) availabl from NSG America, Inc., in the optical system of the automated DNA sequencing machines allows an image to be focused onto the fluorescence detector with a near unity magnification ratio. The most important advantage of utilizing such lens arrays for the detection of fluorescence in low light intensity conditions lies in their high numerical aperture which enables them to transmit a greater percentage of fluorescent light to the detector than the more traditional lenses used in this application.

Other advantages of such lens arrays lie not only in th fact that they are widely used and so affordable, but also in that their flexibility allows them to be utilized equally well with a variety of detection systems including the CCD or diode/amplifier-based detection systems.

As with all standard optics, the characteristic brightness of the SLA is given by the numerical aperture (NA). The SLA can operate in two modes - a field or line scanning mode. The NA of the line scanning mode is always higher than that of the field scanning mode. When used with the CCD-based detector system, the SLA operates in a line scanning mode. Due to the small pixel size of the CCD, e.g. 50 um, the detector "sees" only a line. In contrast, when the SLA is used in conjunction with the diode/amplifier array, it uses the field scanning mode. This, again, is a function of pixel size because the diode has a much larger pixel size than the CCD, e.g. 3 mm, the detector thus "sees" a greater area.

GRIN lenses such as the SLA are typically composed of one or more rows of SELFOC graded-index micro lenses, each with equal dimensions and identical optical properties. The individual lenses which make up the SLA are aligned between two fiberglass-reinforced plastic plates. The interstices are filled with black silicone. The use of black silicone not only protects the individual lenses, but also prevents flare or crosstalk between the lenses. A continuous 1:1 image is

formed by overlapping the images from the adjacent 1 ns elements in the SLA.

The SLA has been used as an optical scanning device in copiers, FAX machines and printers. As discussed previously, it offers significant optical advantages in its high aperture, simplified system for 1:1 imaging and high image quality with no peripheral distortion, as well as in the production of erect, real images. When its better optical properties are combined with manufacturing advantages such as linear construction, easy placement (suited to automatic component assembly), and small size and light weight - lens arrays of the SLA-type are well suited to their application in DNA sequencing machines.

Also anticipated in the scope of the present invention are improvements in the current generation of lens arrays. Newly developed technologies such as those based on lithography, diffusion of metal ions, heat treatment, high precision molding, binary optics and holographics will also have an impact on lens array development. Although lens arrays manufactured using some of the newer technologies suffer from more cross talk than the GRIN lens arrays, it is expected that ultimately such technologies will lead to practical devices which fall within the scope of this invention.

SLA-CCD FLUORESCENCE DETECTION SYSTEMS

A variety of approaches may be used to achieve increased horizontal resolution in systems which utilize CCD detectors. For example, a line- or area-scan camera can be incorporated into the design of the DNA sequencing machine. However, such cameras like some of the automated DNA sequencing machines described thus far, utilize an image reduction CCD, i.e. a camera lens images the object onto a CCD that is considerably smaller than the object. The increased horizontal resolution obtained from this design is offset by the low light collection efficiency of the lens - light is lost in the "demagnification" step which is required for fluorescence

detection by the CCD. Contact imaging CCDs, however, are the same size as the object and, when used with high numerical aperture lens arrays, such as the SLA, do not share the image reduction CCD's limitation of low light collection efficiency.

The combination of the CCD detector and SLA in a DNA sequencing machine offers a number of significant advantages over DNA sequencing systems of the prior art with regard to the overall efficiency of data collection and interpretation. The SLA allows for up to 10 times more fluorescent light to be captured by the detection system. The fact that the lens array provides 1:1 imaging with high numerical aperture enables the CCD to operate with significantly increased sensitivity.

One advantage of the SLA-CCD detector combination, and one unexpected from a review of the prior art, is the ability of the CCD to function efficiently without the inclusion of cooling means in the apparatus. Although the SLA allows for significantly increased amounts of light to be focused on the CCD, the signal to noise ratio of the CCD remains within acceptable limits without the need to provide cooling. Provision of cooling means leads to a further improvement in the signal to noise ratio. The fact that acceptable results can be obtained without the requirement for cooling affords reductions in the cost and complexity of manufacturing the DNA sequencing machine.

As a result of the increased sensitivity imparted to the system by use of the combination of lens array and CCD-based detector, more reliable quantitative information can be obtained from the electrophoresis of DNA samples through the matrix of a gel. For example, compensation can be made for artifacts produced by suboptimal electrophoresis conditions such as globular bands, sloping bands, intralane smiling and uneven distribution of sample across lanes. In this way, reliable DNA sequence information can be obtained from electrophoresis conditions which would otherwise have yielded ambiguous data.

However, the utility of data generated by a DNA sequencing apparatus which utiliz s the SLA-CCD det ctor combination is not limited to the increased accuracy of the DNA sequence information obtained. For example, the better quantitation of DNA in individual bands which is obtained from the combination can be used to provide data on the efficiency of the enzyme utilized in the sequencing reaction as well as data regarding the local structure of the DNA strand being sequenced. Such information can be employed by modern data analysis algorithms to further enhance the efficiency of methods used to decipher stretches of ambiguity in the base sequence as read from the electrophoresis of labeled DNA fragments through a gel matrix. Other areas where the data generated by the system of the present invention are invaluable are those involving allele analysis and fragment mapping, detection of heterozygotes and analysis of viral mutations and populations.

The system therefore has numerous applications in a variety of areas including, but not limited to, paternity testing procedures, forensic medicine, clinical evaluation of disease and cancer-inducing mutations in genes, evaluation of anti-viral drug resistance-inducing mutations during treatment regimens, protein/DNA interaction analysis, and bacterial fingerprinting, in addition to de novo DNA sequencing.

The DNA sequencing machines using SLA-CCD fluorescence detector systems will not only be able to adapt to improvements in gel electrophoresis, but, as previously alluded to, will actually be made more efficient by their implementation. Improvements in present electrophoresis techniques such as those concerning gel composition, loading and electrophoresis conditions will, for example, lead to decreased band width. Some presently available DNA sequencing machines are limited in their vertical resolution and would therefore be unable to take advantage of such improvements. In the system of the present invention, however,it is the means of detection, and not the laser beam, which defines the detector spatial bandwidth of the system. For this reason,

the system's resolution has the potential to be increased by improvem nts in electrophoresis t chnology with the ultimate result that it will have the ability to read sequence data reliably beyond 1000 bases in an acceptable time. This capability results from not only an increased detector resolutior, but also reduced residence time in the gel. Assuming that the loading band is optimally narrow this combination leads to reduced diffusion and thus reduced band width.

In the present multi-photodiode instruments, the laser beam can wander in the vertical plane within wide limits without affecting sensitivity. This advantage occurs as a result of the relatively large aperture of the emission path. However, in the case of the 1:1 imaging CCD, the CCD becomes the limiting aperture in the system (typically this is a function of the CCD pixel size which is of the order of 50 um in the vertical dimension). Thus the laser must be precisely aligned to the detector by, for example, the use of an actuated mirror at the entrance to the gel. An alignment error signal can be derived either from pixels at each end of the CCD or through diodes dedicated for this purpose. The tendency of the laser to wander is a major factor in determining whether alignment must be an ongoing process during electrophoretic separation of the labeled DNA fragments. Laser wandering can be a function of gel composition and/or the laser/dye combination. When using lasers at the red end of the spectrum, for example, an initial adjustment at the beginning of the electrophoresis separation is all that is required.

The diode lasers available in the red and NIR region of the spectrum are capable of high frequency 100% modulation which allows for simple multiwavelength excitation. Two or more laser beams of different wavelength can be launched coaxially through the gel from one or both sides. One hundred percent modulation of the lasers allows each laser beam to share the same spatial path while being separat d in time. This allows for considerable simplification of detector design. Since the

laser beams are not separated in space like the detector of the '148 patent, signals are superimposable in time and emitted fluorescent light is collected efficiently and refocused approximately 1:1 through filters onto either the single or multiple line CCDs mentioned above.

Several recent technological developments in the area of laser diodes, red and near infra-red (NIR) fluorescing dyes, multicolor scanners and optical filter design allow for further increase in the performance of the detection system of the current invention.

Contact imaging CCDs for color scanning are available currently in two configurations: three line CCDs, each line with its own bandpass filter to screen out unwanted wavelengths of light; and single line CCDs, with alternating stripes of bandpass filters. CCDs of either type, with only minor modifications, e.g. matching the bandpass filters to the dyes chosen, allow multiple dye detection. Alternatively, multi-notch filters in combination with single line CCDs also allow use of more than one excitation wavelength.

Another advantage of a DNA sequencing apparatus which incorporates the SLA-CCD detection system arises from the fact that the vertical and horizontal resolution is not limiting. As a result, there are more lanes on the gel available for loading of sample and so more information can be obtained from a single gel.

DIODE/AMPLIFIER FLUORESCENCE DETECTION SYSTEMS

As discussed earlier, the ability to integrate signal amplifier and diode into a single modular structure or alternatively, manufacture a diode array assembly associated with multiple external amplifier devices, has allowed the diode/amplifier-based fluorescence detection systems to overcome some of the physical constraints which had previously limited their use in DNA sequencing machines. The more compact structure of the new diode/amplifier combinations enables the entire gel width to be covered by detectors. In

addition, th stacking height of th detector is less than 5 mm. This imparts the ability to design a DNA sequencing machine which uses non-coaxial beams capable of analyzing two or more dyes in a system where light from the lasers may be coupled through a single standard light coupling plate which minimizes the time delay between the two beams.

The lens arrays contained in DNA sequencing machines which utilize SLA-diode/amplifier detection systems usually contain approximately six rows of GRIN lenses. The exact number of rows is a function of detector pixel size (dimensions parallel to the direction of DNA migration).

As mentioned above, the SLA operates in a field scanning mode when combined with the diode/amplifier detection systems. One of the main advantages of utilizing a detection system for biological molecules such as DNA which contains an SLA in combination with a diode/amplifier detection system lies in the system's dynamic range, a product of the system's increased observation volume compared to that of the CCD-lens array combination. Unlike the apparatus containing the SLA-CCD combination, the SLA-diode/amplifier apparatus tolerates laser movement because of its relatively large field of view (as discussed before, this is a function of the pixel size, e.g. approximately 3 mm in the photodiode/amplifier compared to 50 um in the CCD).

Another advantage to the SLA-diode/amplifier combination detection systems is found in the use of wide gels with high sample capacity for electrophoresis and in instances where so-called laser "bending" occurs. Laser bending usually occurs during electrophoresis when the laser has been engaged for periods of about 2 hours. The beam will bend upwards if the laser was initially pointing up; bend downwards if it was initially pointing down; and will occur even if the laser was pointing only slightly up or down at the time that scanning was initiated. Bending cannot be corrected by adjusting the incident angle of the laser. Although bending disappears within 2 minutes of the electrophoresis being stopped, it will

reapp ar when th electric field is turned on again. The only way to pr vent continu d bending is t change the g l's position so that the laser beam can contact a new and unaffected portion of the gel.

As alluded to in the discussion of the SLA-CCD combination, laser beam bending has been found to be dependent on the type of gel matrix and the laser/dye system being used. For example, bending occurs most strongly when fluorescein is excited by an Argon laser (488 nm); to a lesser extent when tetramethylrhodamine is excited by a He-Ne laser (543 nm); only minimally when Texas Red is excited by a yellow HeNe laser (594); and imperceptibly at 633 nm with CY5 dye. Samples which migrate through the gel close to the point of laser entry are affected to a lesser degree than those in the opposite part of the gel.

The SLA-diode/amplifier combination is advantageous in counteracting the deleterious effects of laser bending in that the field of view of the detector encompasses all but large deviations of the laser beam. This advantage is limited, however, to those instances, discussed above, where laser bending is problematic.

Although it has many advantages, the SLA-diode/amplifier combination is still costly and has limitations in terms of vertical and horizontal resolution. Furthermore, a DNA sequencing machine containing the combination will not be able to adapt to the improvements in gel technology noted above in the discussion of the SLA-CCD combination.

Although both combinations give rise to DNA sequencing machines which are improvements over the prior art, each of the two combinations of SLA (with diode/amplifier or CCD detectors) has advantages and disadvantages associated with its use. Depending on the relative importance of a number of factors, including cost, sensitivity, the degree of horizontal and vertical resolution required, as well as factors associated with beam wandering (a function of laser wavelength, gel type, and dye), either combination may be more

or less preferable. The incorporation f the SLA into the design of the DNA s quencing machine is a key element enabling the various improvements.

BRIEF DESCRIPTION OF THE DRAWING

Figure 1 is a sketch showing the layout of the laser, optical, CCD detector and data collation components of the apparatus for gel electrophoresis of the present invention.

Figure 2(a) is a schematic diagram showing the arrangement of beam sensing pixels on the CCD element and the composition of the feedback loop system for the detection and correction of beam wandering.

Figure 2(b) is a schematic diagram showing the arrangement of position sensitive diodes on the CCD element and the composition of the feedback loop system for the detection and correction of beam wandering.

Figure 3(a) is a sketch showing the layout of the laser, optical, CCD detector and data collation components of the apparatus for gel electrophoresis of the present invention in which light from two separate laser light sources irradiate the gel electrolyte layer of the electrophoresis gel at two distinct regions.

Figure 3(b) is a sketch showing the layout of the laser, optical, CCD detector and data collation components of the apparatus for gel electrophoresis of the present invention in which light from three separate laser light sources are combined so that the gel electrolyte layer of the electrophoresis gel is irradiated at a single region.

Figure 4(a) is a schematic diagram of the arrangement of color filters on a single line CCD element.

Figure 4(b) is a schematic diagram of the arrangement of color filters on stacked CCD elements.

Figure 5 is a sketch showing the layout of the laser, optical, photodiode/amplifier detector and data collation components of the apparatus for gel lectrophoresis of the pres nt inv ntion.

Figur 6(a) is a schematic diagram of the arrangement of the photodiode and amplifier compon nts in the integrated photodiode/amplifier module detector of the present invention.

Figure 6(b) is a schematic diagram of the arrangement of the photodiode and amplifier components of the non-integrated photodiode/amplifier detector of the present invention.

Figure 7 is a sketch showing the layout of the laser, optical, photodiode/amplifier detector and data collation components of the apparatus for gel electrophoresis of the present invention in which light from two distinct laser light sources irradiate the gel electrolyte layer of the electrophoresis gel at two distinct regions.

Figure 8(a) is an example of the output of the embodiment of the present invention which utilizes a CCD detector and is described in Figures 1 to 3.

Figure 8(b) is an example of the output of the embodiment of the present invention which utilizes a photodiode/amplifier detector and is described in Figures 5 to 7.

DESCRIPTION OF PREFERRED EMBODIMENTS OF THE INVENTION

Preferred embodiments of the invention incorporate a number of features. The specific form of those features presented in the preferred embodiments of the invention are in accordance with its use as an apparatus for the determination of the sequence of DNA, specifically for the determination of sequence information from the separation of fluorophore-labeled DNA fragments prepared using the method of Sanger et.al.. This application has been selected because of its widespread use and importance. In other applications, other specific forms may be preferable.

Reference will now be made to the drawings, whereby like parts are designated by like numerals.

With reference to Figure 1, samples are loaded into a predetermined number of sample loading wells 10 situated at the top of a polyacrylamide gel 16 contained in an electrophoresis apparatus 12 consisting of components well

known to th s skilled in the art and assembled according to standard procedur s. The polyacrylamid gel is immersed at its opposite ends in an electrolyte in electrode tanks. A voltage, applied across the electrode tanks by means of a power supply, causes the samples to migrate within the gel electrolyte layer 16. The samples migrate in a downward direction through the gel electrolyte layer 16 situated between two electrophoresis plates 17', 17'' so that a plurality of parallel migration lanes 18 form. These parallel migration lanes 18 substantially correspond to the positions of the sample loading wells 10.

Light from a single laser light excitation source operating in the wavelength range 400 to 900 nm, 19 (such as a He-Ne laser operating at a wavelength of 633 nm) is focused by a condenser lens 20 and finally steered through a beam director 21 so that it is launched into the gel electrolyte layer 16 situated between two electrophoresis plates 17', 17'' at a predetermined linear irradiation region 22. When light from the single laser light excitation source 19 excites the fluorophore-labeled DNA fragments 23 migrating through the gel electrolyte layer 16 situated between two electrophoresis plates 17', 17'', fluorescent light is emitted from the fluorophore-labeled DNA fragments 23. The fluorescent light emitted from the excited fluorophore-labeled DNA fragments 23 falls on a light collection and focusing lens array 24 which is situated in a posterior position relative to the electrophoresis plates 17', 17'' and extends in a direction parallel to the linear irradiation region 22. The fluorescent light emitted from the excited fluorophore-labeled DNA fragments 23 is collected by the light collection and focusing lens array 24 and focused onto a filter arrangement 25 and then onto a CCD element 26.

The light collection and focusing lens array 24 consists of an array of gradient index lenses composed of individual SELFOC graded-index micro lenses 28 of substantially equal dim nsion and substantially identical optical properties. The

individual lenses 28 are aligned betwe n two fiberglass-r inforced plastic plates 29, 30. The interstices 31 are filled with black silicone.

The gradient index lens array provides near unity magnification of light focused onto the CCD element 26. The CCD element 26 is divided into a plurality of photosensitive cells or pixels 32.

As the temperature rises, an increasing amount of dark current will flow through the CCD element 26 and thereby reduce its efficiency. In order to alleviate this problem, the CCD element 26 can be adapted to be cooled with the Peltier device 33 so that it will, at all times, be operational within a predetermined temperature range. To enhance the cooling efficiency, a heat sink 34 is included with the Peltier device 33.

The fluorescent line images collected and focused onto the CCD element 26 by the light collection and focusing lens array 24 are converted to electrical signals which are then displayed on a monitor 36 and fed to a controller 35 and a digital data processor 37. The digital data processor 37 monitors temporal alterations in the intensities of the fluorescent line images and feeds the results to a device such as a printer 38 which reproduces data in readable form.

For certain applications, it may be preferable to maintain the beam from the laser light excitation source 19 within precise limits to prevent beam wandering. As shown in Figure 2(a), this can be accomplished by including dedicated beam sensing pixels 39 or, as shown in Figure 2(b), separate position sensitive diodes 40 at opposite ends of the CCD element 26. Signal from the beam sensing pixels 39 or position sensitive diodes 40 can be used to control other components well known to those skilled in the art, such as a laser beam director 41 or detector position actuators 42, in a feedback loop system in order to maintain the beam from the laser light excitation source 19 within predetermined limits with respect to the detector means 26.

In other applications it may be preferable to utilize more than on laser light xcitati n source. M ans of multiple laser light excitation are shown in Figures 3(a) and 3(b). Figure 3(a) depicts a system in which excitation is accomplished by the utilization of two separate laser light sources 19, 19'. Light from the two laser light excitation sources 19, 19' strikes the electrolyte layer 16 situated between the two electrophoresis plates 17', 17'' at two distinct, predetermined linear irradiation regions 43, 44.

Fluorescent light emitted by the excited fluorophore-labeled DNA fragments 23 is collected by a light collection and focusing lens array 24 and is focused through light filters 45, 46 and then onto two CCD elements 26, 26'.

Alternatively, as shown in Figure 3(b), light from two or more laser light excitation sources 19', 19'', 19''' can be combined in a beam combining element 47, so that the combined beam strikes the gel electrolyte layer 16 situated between two electrophoresis plates 17', 17'' at a single predetermined linear irradiation region 48.

Fluorescent light emitted by the excited fluorophore-labeled DNA fragments 23 is collected and focused by a light collection and focusing lens array 24 and is focused through a multiple notch light filter 52 and then onto a single CCD element 26.

For either apparatus depicted in Figures 3(a) or 3(b) the CCD element can be cooled by Peltier device 33 and associated heat-sink 34.

Fluorescent light emitted by the excited fluorophore-labeled DNA fragments 23 in the apparatus depicted in either Figure 3(a) or 3(b) can be detected by matching multiple CCD elements 26, 26' with specific color filters 45, 46 or by th utilization of CCD elements 26 modified by the incorporation of multicolor filters 50 deposited on the CCD element 26 by techniques well known to those skilled in the art.

In Figure 4(a) multicolor filters 50 are shown as filters 101, 102, 103 in a single line CCD element 26. Alternatively,

as shown in Figure 4(b), the CCD elements can be stacked closely together on the same substrate and single color filter 201, 202, 203 used to coat each CCD element. Depending on beam dimensions, this combination could be used in conjunction with the laser configuration of Figure 3 or Figure 7.

In another separate embodiment of this invention, shown in Figure 5, samples are loaded into a predetermined number of sample loading wells 10 situated at the top of a polyacrylamide gel 16 contained in an electrophoresis apparatus 12 consisting of components known to those skilled in the art and assembled according to standard procedures. The polyacrylamide gel 16 is immersed at its opposite ends in an electrolyte in electrode tanks. A voltage, applied across the electrode tanks by means of a power supply, causes the samples to migrate within the gel electrolyte layer 16. The samples migrate in a downward direction through the gel electrolyte layer 16 situated between two electrophoresis plates 17', 17'' so that a plurality of parallel migration lanes 18 form. These parallel migration lanes 18 substantially correspond to the positions of the sample loading wells 10.

Light from a single laser excitation source 19 operating within the wavelength range 400 to 900 nm (such as a He-Ne laser operating at a wavelength of 633 nm) is focused by a condenser lens 20 and finally steered through a beam director 21 so that it is launched into the gel electrolyte layer 16 situated between two electrophoresis plates 17', 17'' at a predetermined linear irradiation region 22. When light from the single laser light excitation source 19 excites the fluorophore-labeled DNA fragments 23 migrating through the gel electrolyte layer 16 situated between the two electrophoresis plates 17', 17'', fluorescent light is emitted from the fluorophore-labeled DNA fragments 23. The fluorescent light emitted from the excited fluorophore-labeled DNA fragments 23 falls on a light collection and focusing lens array 24 which is situated in a posterior position relative to the

l ctrophor sis plate 17', 17'' and xtends in a dir ction parallel to th linear irradiation r gion 22. The fluorescent light emitted from the excited fluorophor -labeled DNA fragments 23 is collected by the light collection and focusing lens array 24 and focused onto a filter arrangement 25 and then onto a into a photodiode/amplifier assembly 55.

The light collection and focusing lens array 24 consists of an array of gradient index lenses composed of individual SELFOC graded-index micro lenses 28 of substantially equal dimension and substantially identical optical properties. The individual lenses 28 are aligned between two fiberglass-reinforced plastic plates 29, 30. The interstices 31 are filled with black silicone.

The gradient index lens array provides near unity magnification of light focused onto the photodiode/amplifier assembly 55.

As shown in Figures 6(a) and 6(b), the photodiode/amplifier assembly 55 can be configured in two ways. In Figure 6(a) the photodiode/amplifier assembly 55 consists of one or more rows of integrated photodiode/amplifier modules 56. The individual integrated photodiode/amplifier modules consist of a signal amplifier 58 in combination with the electronics required for signal multiplexing 59 and a diode chip 60. The individual diode chips 60 each contain a single pixel 61 of uniform size.

The photodiode/amplifier assembly 55 shown in Figure 6(b) consists of distinct amplifier and diode modules 62, 63, respectively. The diode module 63 consists of one or more rows of photodiodes 61, of uniform size.

The diode module 63 is associated with the amplifier module 62. The amplifier module 62 consists of integrating detector amplifiers 58 and signal multiplexer 59.

In certain applications, it may be preferable to utilize two or more las r light xcitation sources 19 to excite the fluorophore-labeled DNA fragments 23 as they migrate through

the gel electrolyte layer 16 situated between two electrophoresis plates 17', 17''. Figure 7 shows two individual laser light excitation sources 19, 19' which strike the gel electrolyte layer 16 situated between the two electrophoresis plates 17', 17'' at two distinct, predetermined linear irradiation regions 43, 44.

Light emitted from the excited fluorophore-labeled DNA fragments 23 is collected by the light collection and focusing lens array 24 and focused through light filters 45, 46 onto two diode/amplifier assemblies 65, 66 situated so that each is able to detect the fluorescent light emitted from one of the linear irradiation regions 43, 44. The filter arrangement 50 has been previously described in Figures 4(a) and 4(b).

Sample output from a detector of the CCD type described in Figures 1 to 3 is shown in Figure 8(a). Sample output from a detector of the multiple diode type described in Figures 5 to 7 is shown in Figure 8(b).

While the invention has been described in terms of certain preferred embodiments, it should be understood that other and further modifications may be made without diminishing the scope of the invention which is set forth in the following claims.

CLAIMS

WHAT IS CLAIMED IS:

1. An improved apparatus for analysis of biological molecules of the type having a gel matrix means for separating labeled biological molecules in electrophoretic pathways by application of an electrical potential means to said gel matrix means, and in which a light generating means excites said labeled biological molecules while they migrate in said gel matrix means, and in which collection and focusing means collect and focus output signals emitted by said excit d biological molecules, and in which a detection means and storage means detect, store and analyze said signals collected from said excitation of labeled biological molecules, characterized in that:

a collection and focusing means comprises a substantially unity magnification lens array for collecting output light signals emitted by said labeled biological molecules and focusing said output signals along a linear area extending transversely across said gel matrix means such that respective pathways of electrophoretic migration can be detected independently of one another.

2. The apparatus of claim 1 wherein said electrical potential means comprises two electrodes coupled to spatially separated portions of said matrix means in a vertical plane.

3. The apparatus of claim 1 wherein said electrical potential means comprises two electrodes coupled to spatially separated portions of said matrix means in a horizontal plane.

4. The apparatus of claim 1 wherein said light generating means comprises laser means.

5. The apparatus of claim 1 wherein said light generating means comprises at least one laser means capable of 100% modulation for coaxially projecting light of different wavelengths onto said gel matrix means.

6. The apparatus of claim 1 wh rein said light generating means comprises at least one laser operating in the wavelength range 400-900 nm.

7. The apparatus of claim 1 wherein light from said light generating means is projected horizontally onto said gel matrix means in a direction which is substantially perpendicular to said electrophoretic pathways of said labeled biological molecules.

8. The apparatus of claim 1 wherein said output from said light generating means is projected in a direction substantially perpendicular to said electrophoretic pathways of said labeled biological molecules.

9. The apparatus of claim 1 wherein labeled biological molecules are excited at a predetermined position along said electrophoretic pathways, said labeled biological molecules emitting a detectable output in response thereto.

10. The apparatus of claim 1 wherein said lens array of said collection and focusing means comprises at least one row of graded-index micro-lenses or focusing means of similar function.

11. The apparatus of claim 1 wherein said lens array of said collection and focusing means comprises a predetermined number of lenses forming an array of sufficient length to detect output signal from opposite ends of a linear irradiation region of said gel matrix means used for separation of said labeled biological molecules.

12. The apparatus of claim 1 wherein said detection means comprises filter means in combination with a CCD sensing means, said CCD sensing means containing sufficient cells to provide output signals from a linear irradiation region of said gel matrix detectable as a predetermined number of pixels.

13. The apparatus of claim 12 wherein said CCD sensing means is operational at ambient temperature.

14. The apparatus of claim 12 wherein said CCD sensing means further comprises supplementary cooling means.

15. The apparatus of claim 1 wherein said detector means is composed of a filter means in combination with at least one

row of diode/amplifier modules, said diodes containing pixels of substantially uniform size.

16. The apparatus of claim 1 wherein said detector means is composed of a filter means in combination with at least on row of diode modules connected to external amplifier modules, said diode modules containing pixels of substantially uniform size.

17. The apparatus of claim 16 wherein said rows of diode/amplifier modules are of a length to detect output signals from opposite ends of a linear irradiation region of said gel matrix means.

18. The apparatus of claim 1 wherein signals from said sensing means are coupled to digital data processor means.

19. The apparatus of claim 1 wherein said label incorporated into said biological molecules comprises at 1 ast one fluorescent dye.

20. The apparatus of claim 1 wherein said label incorporated into said biological molecule is a phosphor.

21. The apparatus of claim 1 wherein said biological molecule is selected from the group consisting of bacteria, nucleic acid and protein.

22. The apparatus of claim 1 wherein said means of separation is selected from the group consisting of capillary means, slab means and channel means.

23. The apparatus of claim 1 wherein a predetermined number of individual lenses located at opposite ends of said lens array in said detecting means are provided for sensing light from said light generating means, said individual lenses forming part of a feedback system to align said light generating means within defined vertical parameters.

24. An improved apparatus for sequencing nucleic acid of the type having a gel matrix means for separating labeled molecules of nucleic acid in electrophoretic pathways by application of an electrical potential means to said gel matrix means, and in which a light generating means excites said labeled molecules of nucleic acid while they migrate in

said gel matrix means, and in which collection and focusing means collect and focus utput signals emitted by said excited molecules of nucleic acid, and in which a detection, storing and displaying means detect, store and display said output signal from said excitation of labeled molecules of nucleic acid, characterized in that said apparatus further comprises:

means for projecting an output from said light generating means in a direction substantially perpendicular to direction of said migration of labeled molecules of nucleic acid; and

a means for collecting and focusing signal emitted from said labeled molecules of nucleic acid onto at least one detecting means, said collecting and focusing means comprising a lens array of at least one row of graded-index micro lenses or focusing means of similar function, said collecting and focusing means providing substantially unity magnification of signal.

25. The apparatus of claim 24 wherein said nucleic acid is selected from the group consisting of DNA and RNA.

26. The apparatus of claim 24 wherein said label comprises at least one fluorescent dye.

27. The apparatus of claim 24 wherein said label is a phosphor.

28. The apparatus of claim 24 wherein said light generating means comprises laser means.

29. The apparatus of claim 24 wherein said light generating means comprises at least one laser means capable of 100% modulation for coaxially projecting light of different wavelengths onto said gel matrix means.

30. The apparatus of claim 24 wherein said light generating means comprises at least one laser operating in the wavelength range 400-900 nm.

31. The apparatus of claim 24 wherein different wavelengths of said output from said light generating means are projected coaxially onto said gel matrix means in a direction which is substantially perpendicular to said electrophoretic pathways of said labeled molecules of nucleic acid.

32. The apparatus of claim 24 wherein light from at least ne said light generating means is proj cted horizontally onto said gel matrix means in a direction which is substantially perpendicular to said electrophoretic pathways of said label d molecules of nucleic acid.

33. An improved method for sequencing labeled molecules of nucleic acid by means of apparatus of the type having a gel matrix means for separating labeled molecules of nucleic acid in substantially parallel electrophoretic pathways by application of an electrical potential means to said g l matrix means, and in which a light generating means excites said labeled molecules of nucleic acid while they migrate in electrophoretic pathways in said gel matrix means, and in which collection and focusing means collect and focus output signals emitted by said excited molecules of nucleic acid, and in which a detection, storing and displaying means detect, store and display said output signal from said excitation of labeled molecules of nucleic acid, characterized in that the method further comprises:

projecting an output from said light generating means in a direction substantially perpendicular to the direction of said migration of said labeled molecules of nucleic acid; and

exciting said labeled molecules of nucleic acid with said light generating means while said labeled molecules of nucleic acid migrate in a predetermined direction in said electrophoretic pathways; and

detecting along a predetermined linear area transverse to said gel matrix means, light signals emitted from said labeled molecules of nucleic acid as a result of excitation by said light generating means, such that signals representative of pixels forming respective pathways of electrophoretic migration can be detected independently of one another.

34. The method of claim 33 wherein said labeled molecules of nucleic acid are selected from the group consisting of DNA and RNA.

35. The method of claim 33 wherein said label incorporated into said molecules of nucleic acid comprises at least ne fluorescent dye.

36. The method of claim 33 wherein said label incorporated into said molecules of nucleic acid is a phosphor.

37. The method of claim 33 wherein said light generating means comprises laser means.

38. The method of claim 33 wherein said light generating means comprises at least one laser capable of 100% modulation such that laser beams of different wavelengths are projected coaxially into said gel matrix means in a direction which is substantially perpendicular to electrophoretic migration pathways of said labeled molecules of nucleic acid.

39. The method of claim 33 wherein light from said light generating means is projected horizontally into said gel matrix means in a direction which is substantially perpendicular to electrophoretic migration pathways of said labeled molecules of nucleic acid.

40. The method of claim 33 wherein said labeled molecules of nucleic acid are excited at a predetermined position along said electrophoretic migration pathway such that said labeled molecules of nucleic acid emit an output signal.

41. The method of claim 33 wherein light signals emitted by said labeled molecules of nucleic acid are collected in a lens array and imaged onto a CCD detector, said lens array providing substantially unity magnification of said light signals.

42. The method of claim 33 wherein light signals emitted by said labeled molecules of nucleic acid are collected in a lens array and imaged onto an amplifier/diode detector, said lens array providing substantially unity magnification of said light signals.

Fig. 1

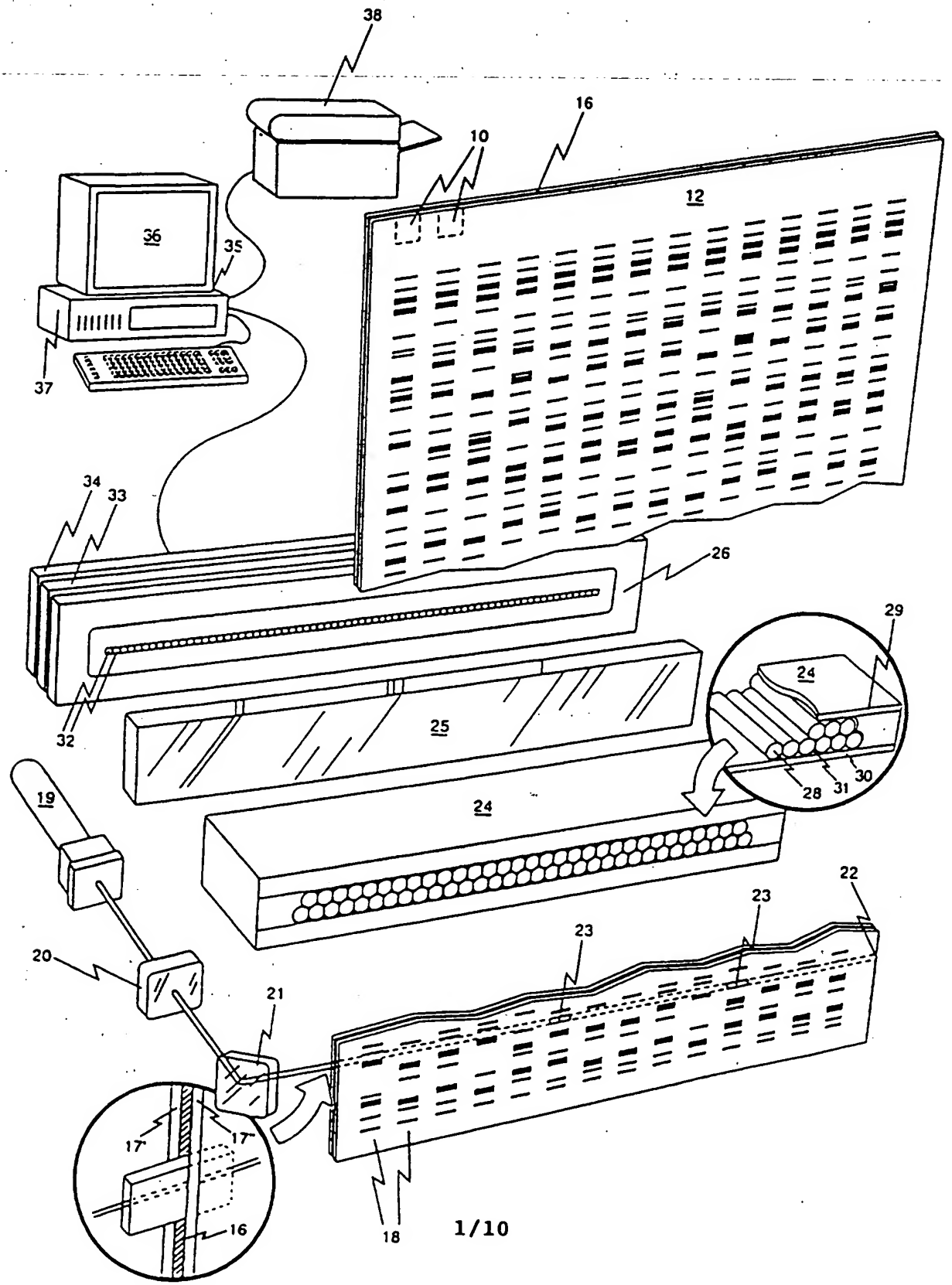
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Fig. 2a

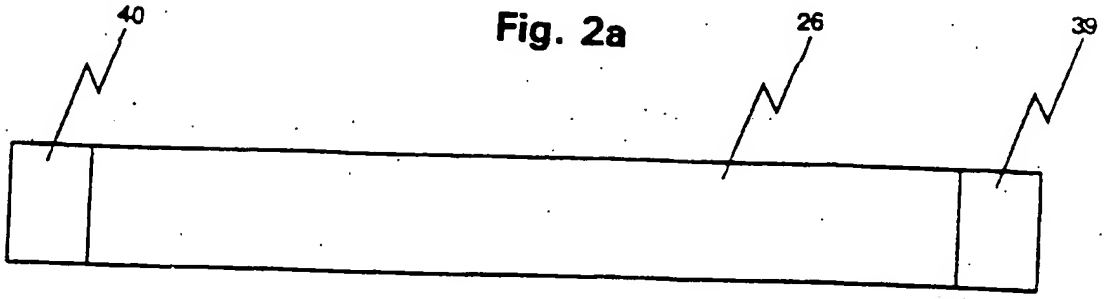

Fig. 2b

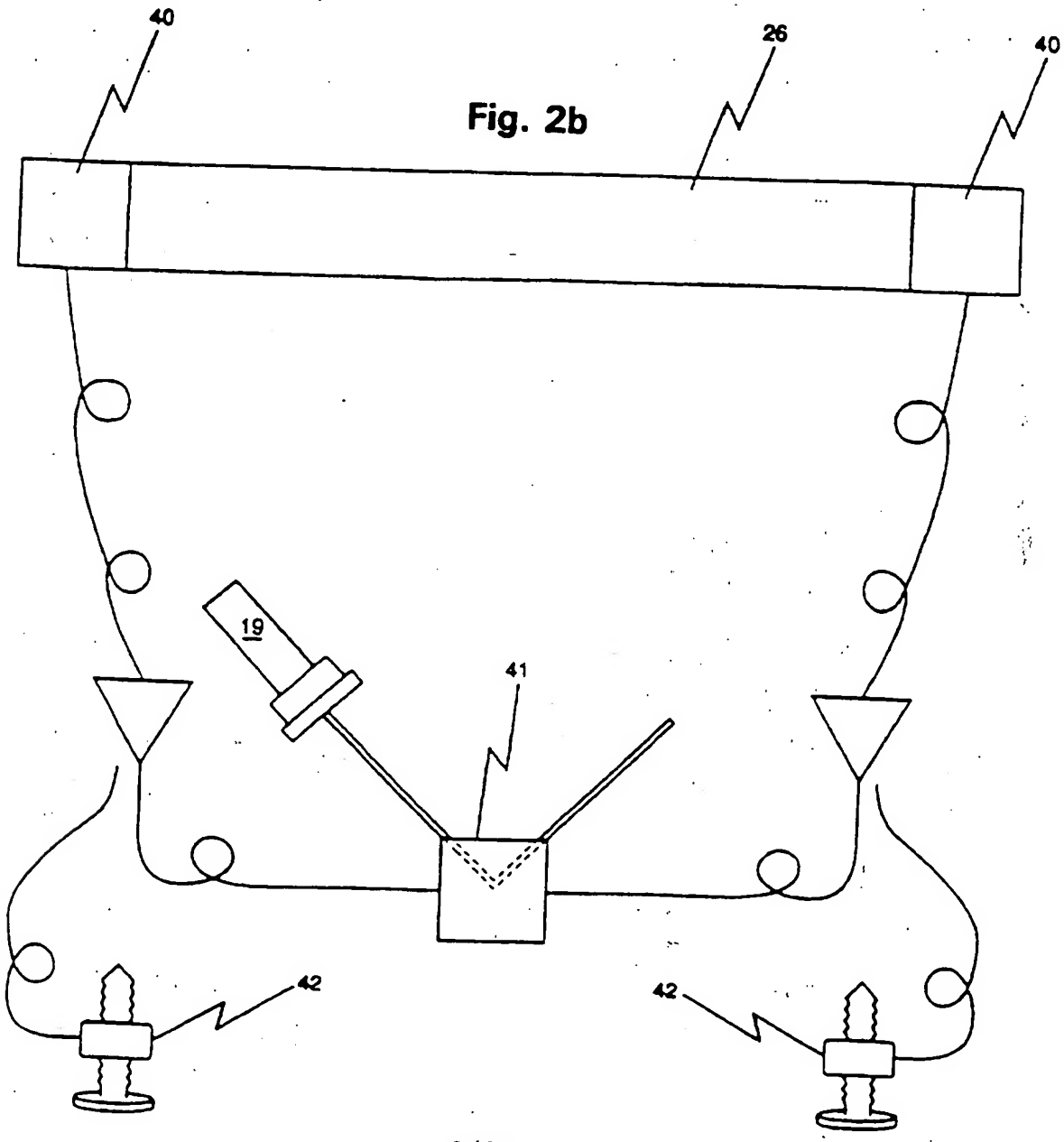

Fig. 3a

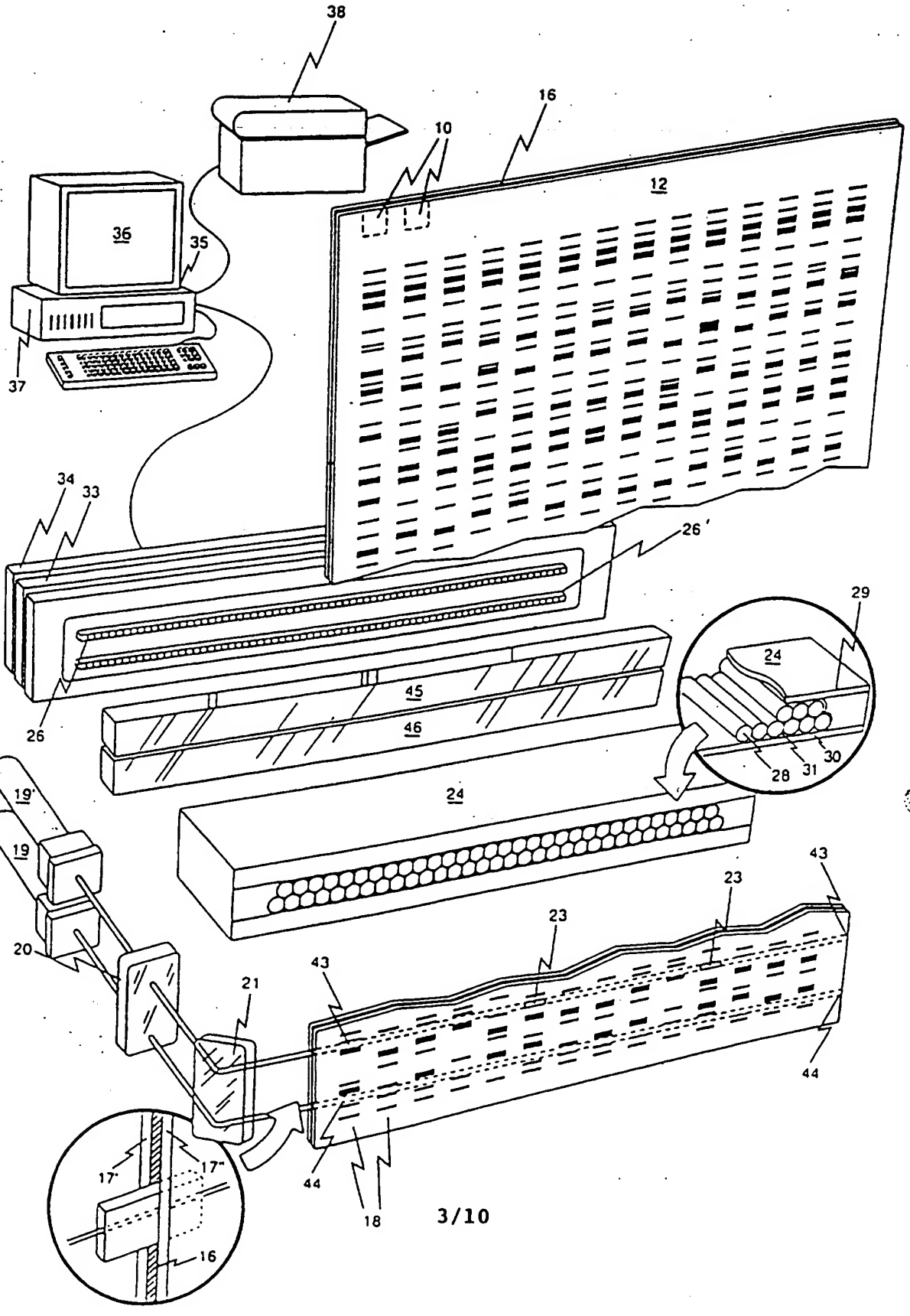
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Fig. 3b

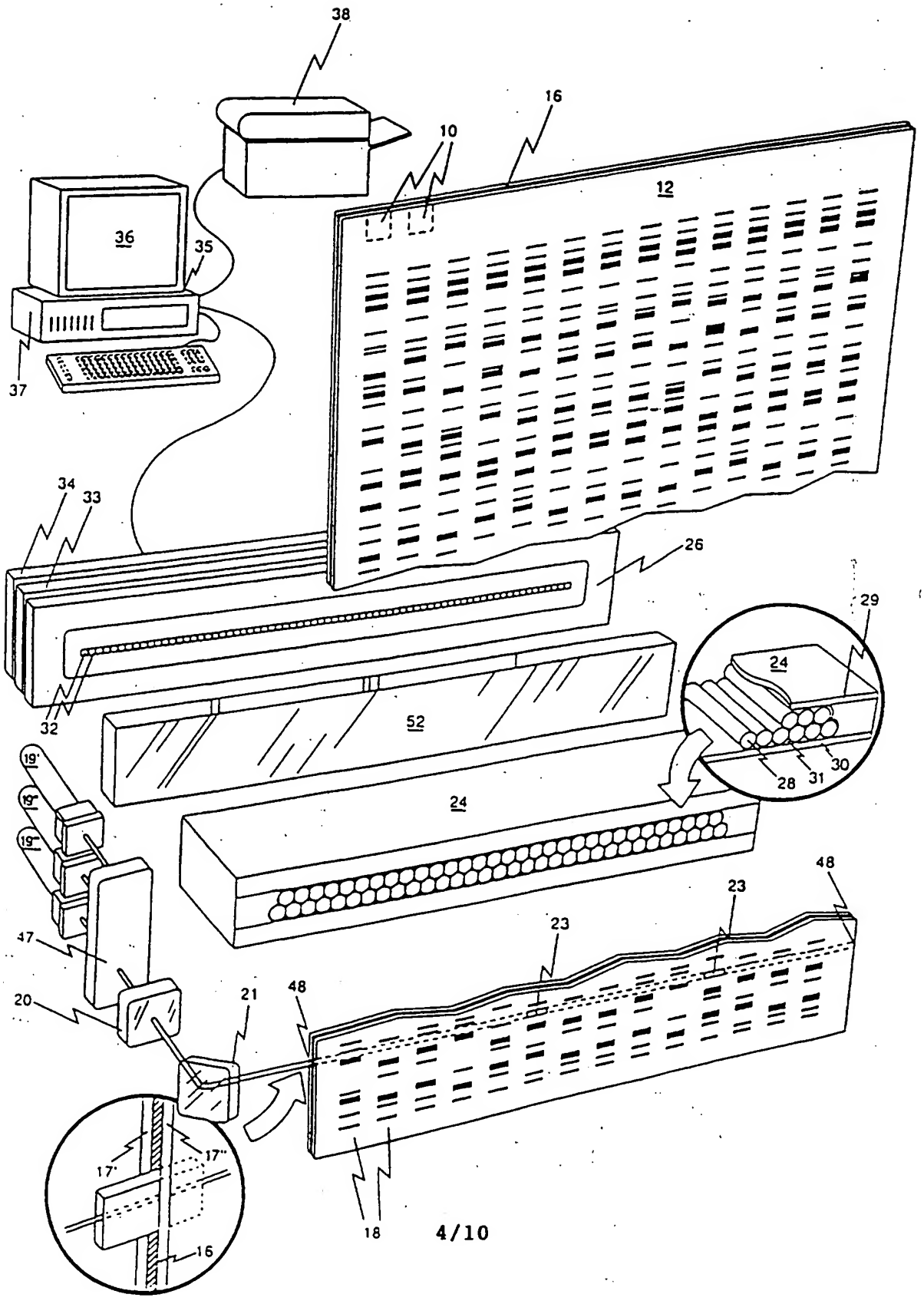
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Fig. 4a

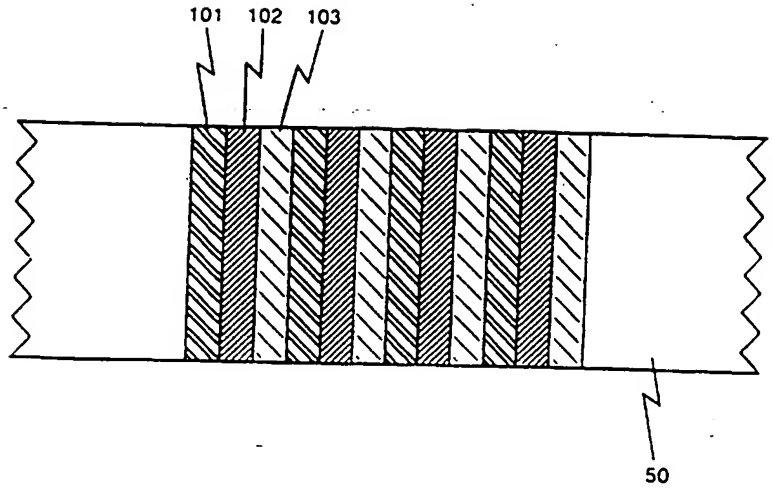

Fig. 4b

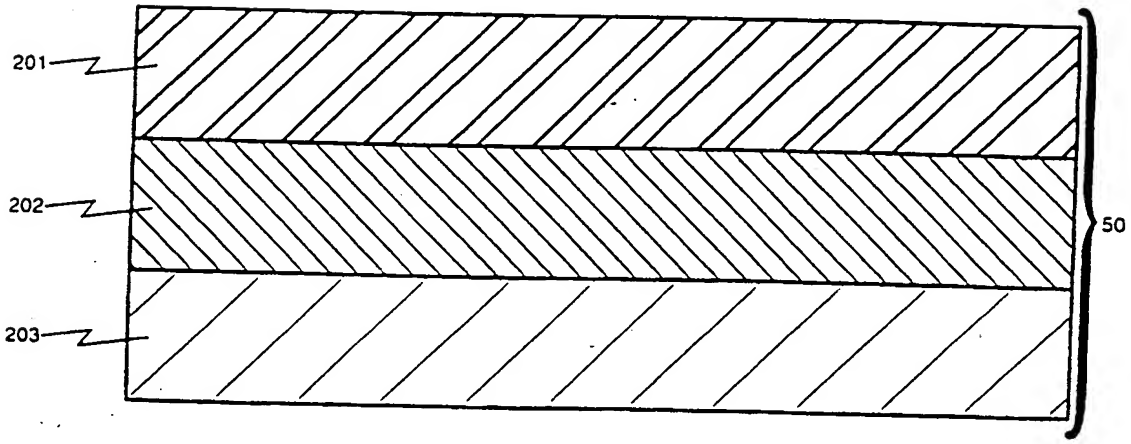

Fig. 5

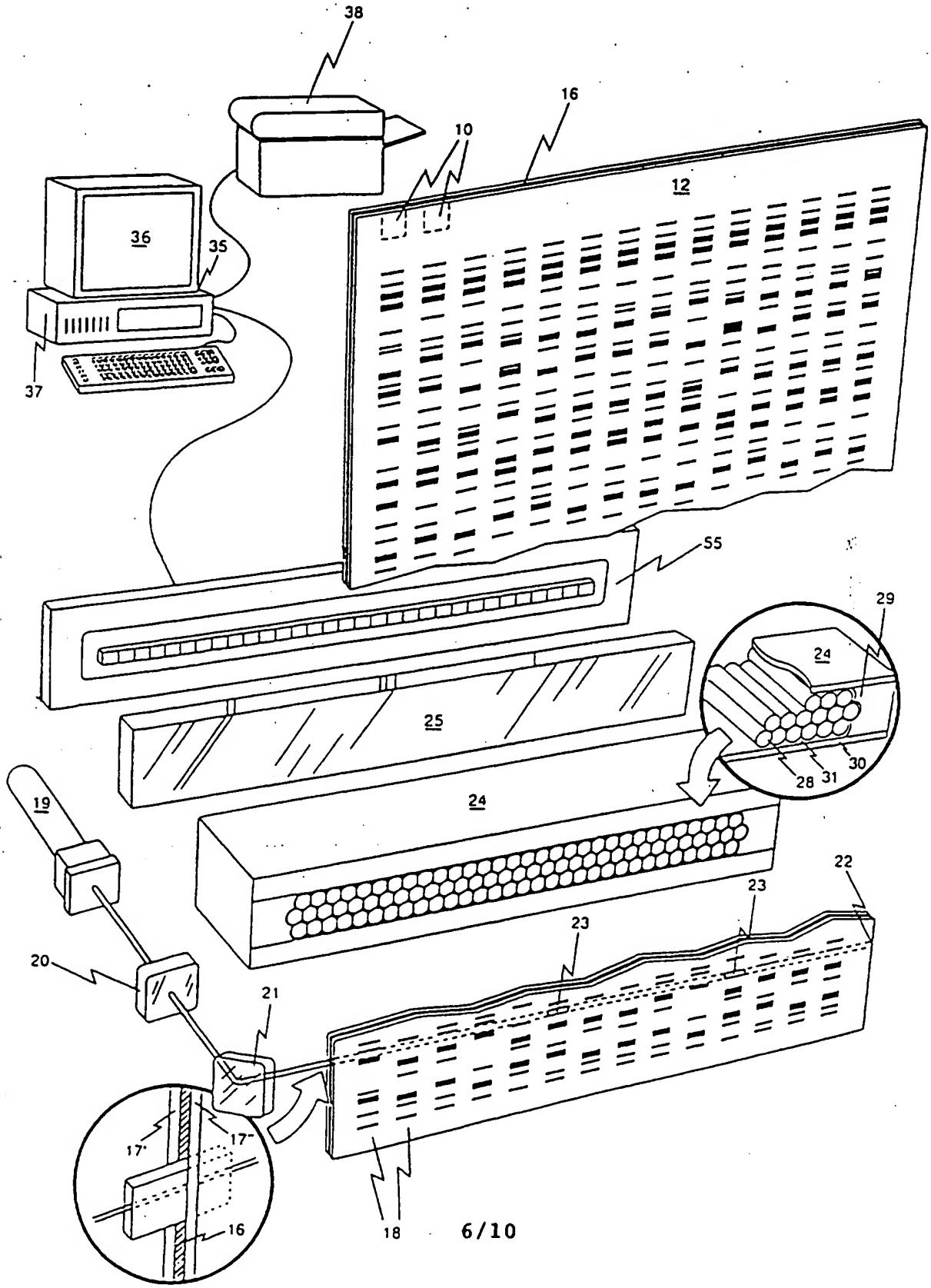
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Fig. 6a

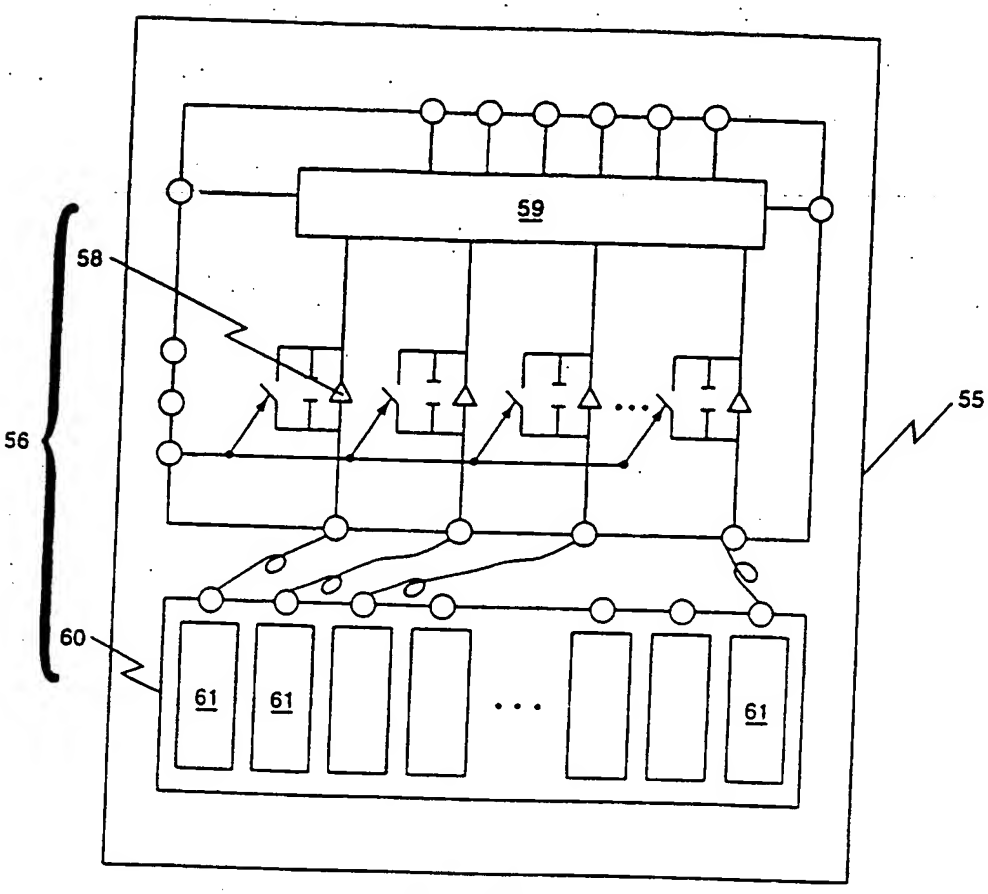

Fig. 6b

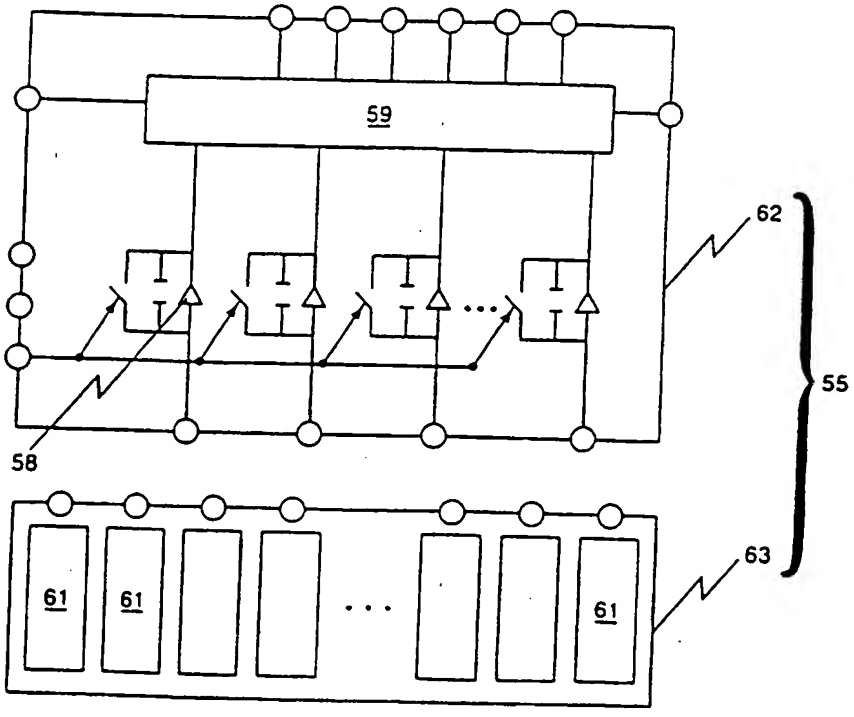

Fig. 7

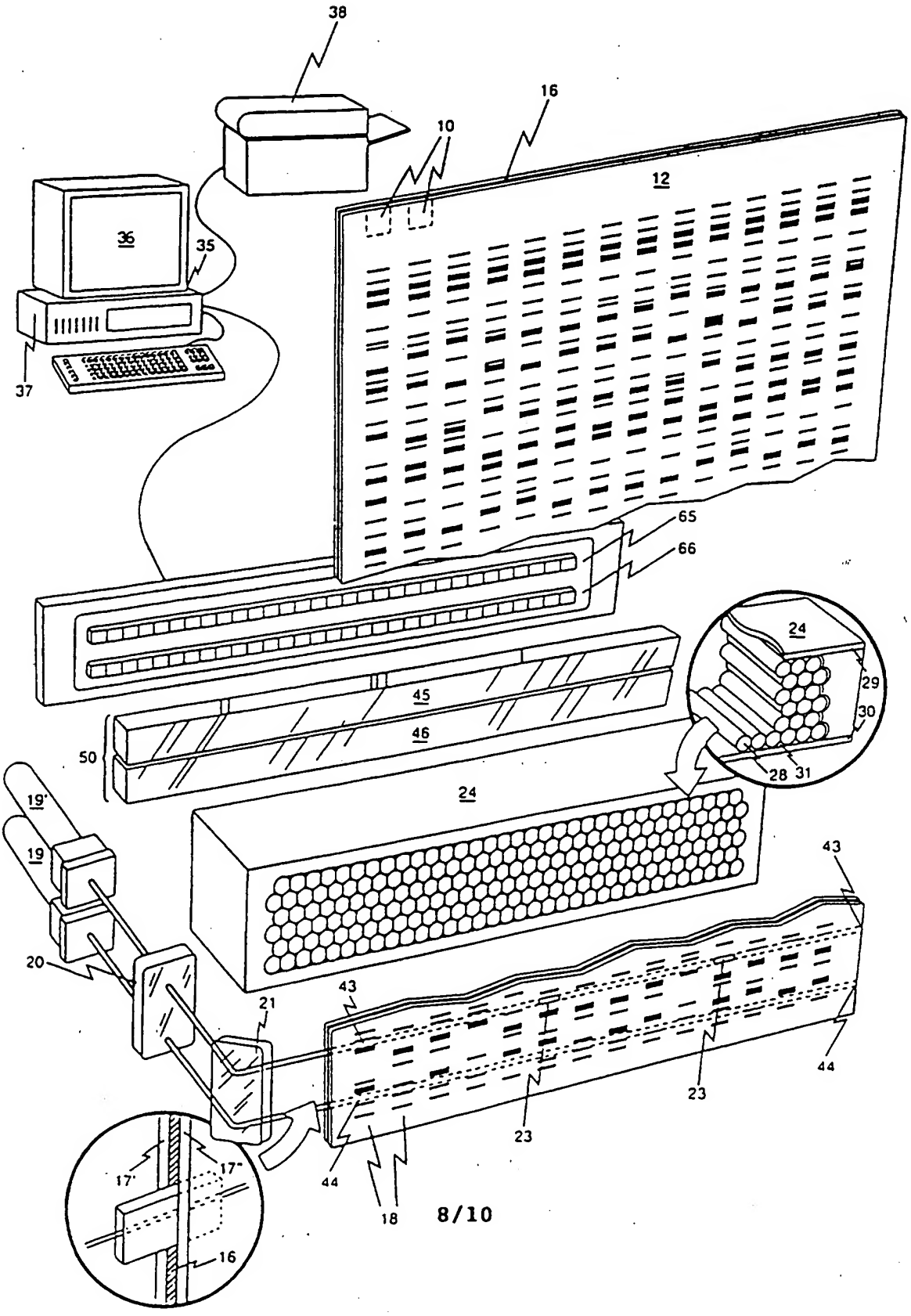
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Fig. 8a

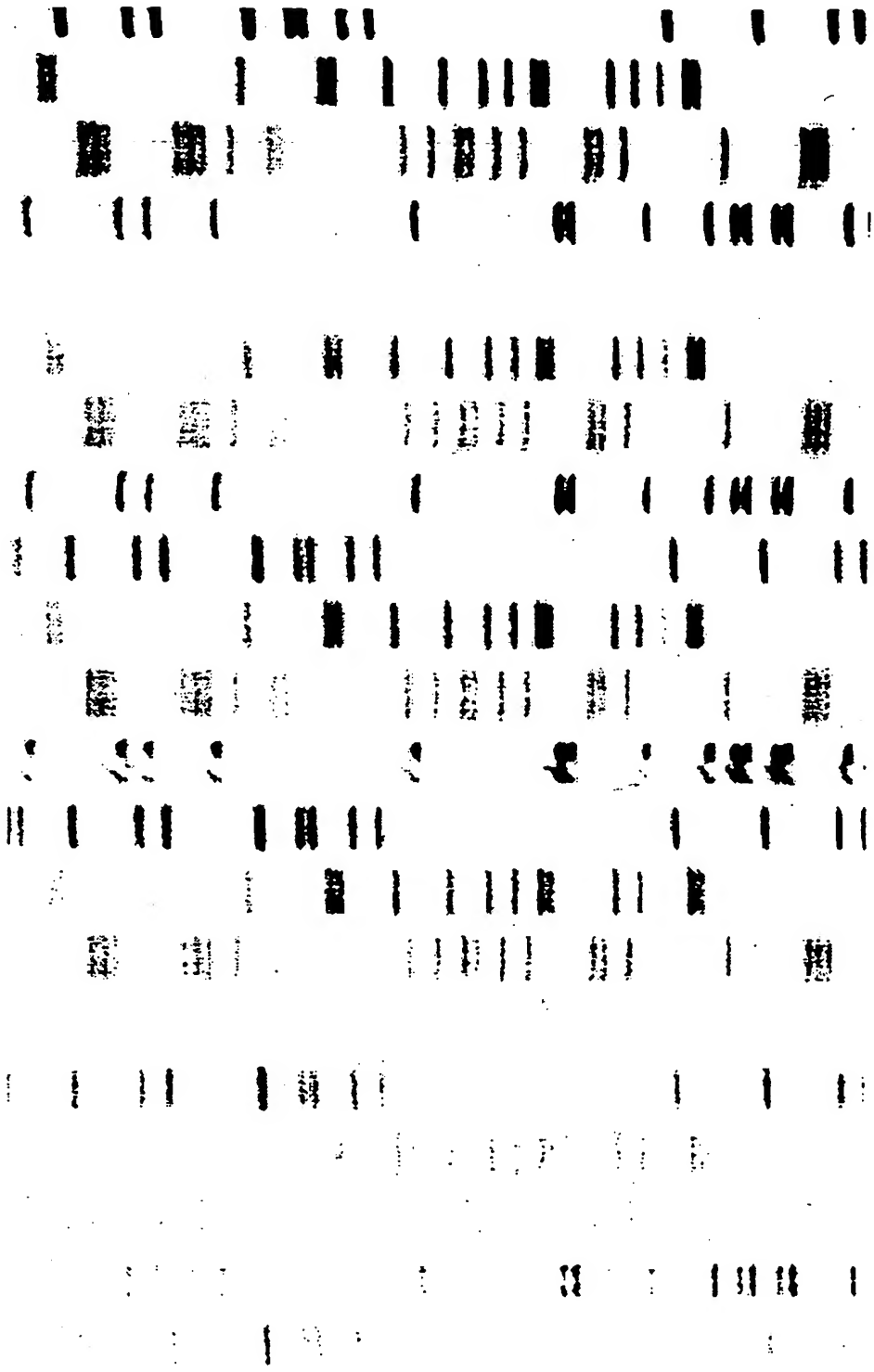
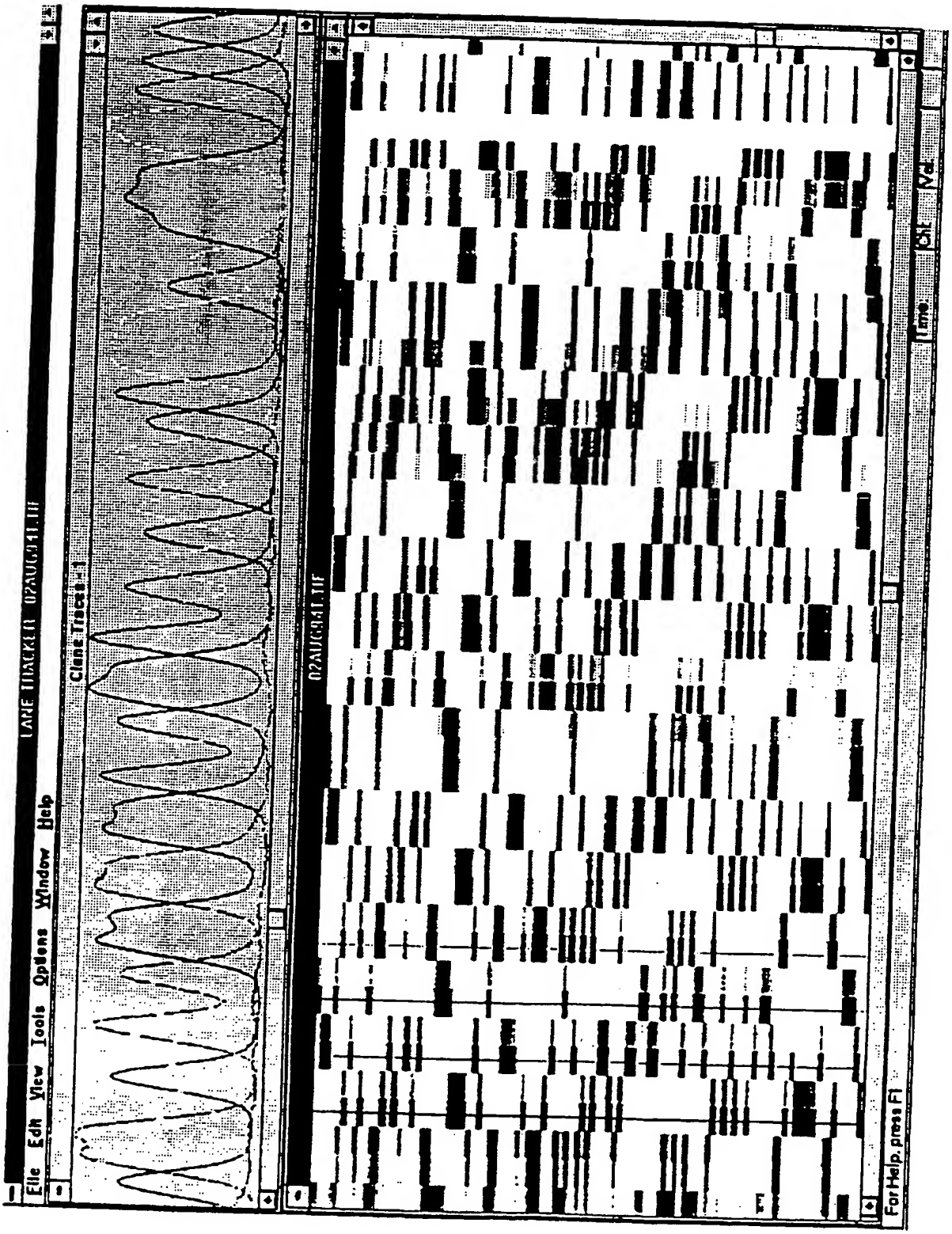


Fig. 8b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INTERNATIONAL SEARCH REPORT

International application No.
PCT/US96/01613

A. CLASSIFICATION OF SUBJECT MATTER

IPC(6) :G0IN 27/26, 27/447
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B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 204/461,612

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
E	EP,A, 0645622 (Hitachi Electronics Engineering Co., LTD) 29 March 1995, see entire document.	1-42
X ---- Y	US,A, 4,971,677 (Kambara et al) 20 November 1990. See entire document.	33-35,37, 39, & 40 ---------- 36,38
X	WO,A, 87/07719 (Europa Sches Laboratorium For Molekularbiologie) 17 December 1987. See entire document.	33-40

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

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08 APRIL 1996	15 MAY 1996
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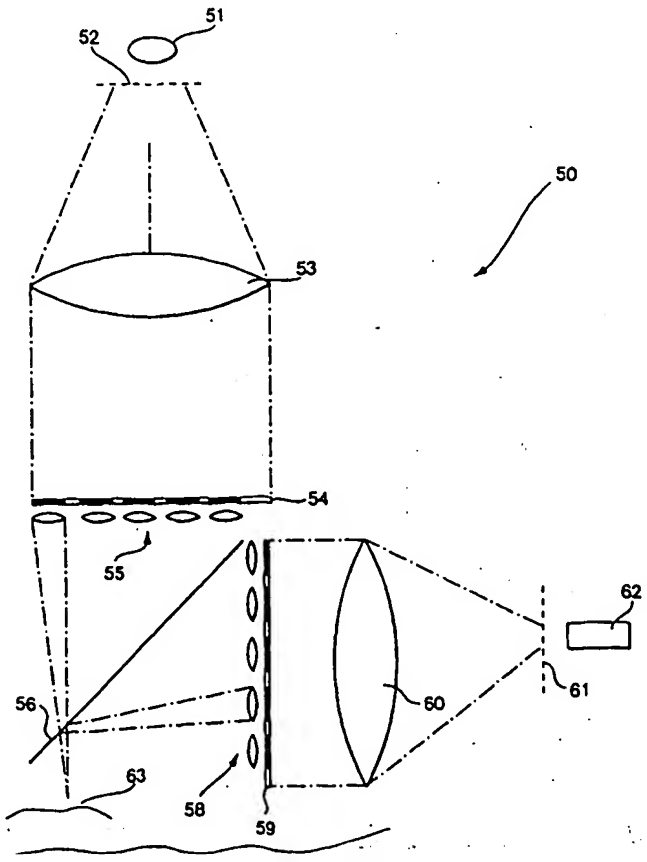
Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.

(54) Title: SPATIALLY RESOLVED OPTICAL MEASUREMENTS

(57) Abstract

Methods and apparatus are provided for determining a characteristic of a sample of a material by the interaction of electromagnetic radiation with the sample. The apparatus includes a source of electromagnetic radiation, an optical assembly and a detector. The optical assembly sequentially illuminates a plurality of volume elements in the sample with an intensity distribution in the sample that drops off substantially monotonically from a first region in a first optical path and collects electromagnetic radiation emanating from each of the volume elements. The optical assembly collects the electromagnetic radiation emanating from each of the volume elements with a collected distribution that drops off substantially monotonically from a second region in a second optical path. The first and second regions at least partially overlap in each of the volume elements. The detector detects the collected electromagnetic radiation emanating from each of the sequentially illuminated volume elements to produce responses representative of the characteristic in each of the volume elements.



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(81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ARIPO patent (KE, LS, MW, SD, SZ, UG), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG).

Published
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(54) Title: MICROLENS SCANNER FOR MICROLITHOGRAPHY AND WIDE-FIELD CONFOCAL MICROSCOPY

(57) Abstract

A microscopy and/or lithography system uses a comparatively low-resolution image projection system, which has a very small numerical aperture but large image field, in conjunction with a microlens array comprising miniature lens elements, each of which has a large numerical aperture but very small field. The projection system contains a small aperture stop which is imaged by the microlenses onto an array of diffraction-limited microspots on the microscope sample or printing surface at the microlens focal point positions, and the surface is scanned to build up a complete raster image from the focal point array. The system design thus circumvents the tradeoff between image resolution and field size which is the source of much of the complexity and expense of conventional wide-field, high-NA microscopy and microlithography systems. The system makes possible flat field, distortion-free imaging, with accurate overlay, focus, and warp compensation, over very large image fields (larger than the practical limits of conventional imaging means). In one embodiment it would use a Digital Micromirror Device as the image source, potentially eliminating the need for photomasks in semiconductor manufacture.

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Veröffentlicht
Ohne internationalen Recherchenbericht und erneut zu veröffentlichen nach Erhalt des Berichts.

(54) Title: ARRAY FOR OPTICAL EVALUATION OF AN OBJECT ARRAY

(54) Bezeichnung: ANORDNUNG ZUR OPTISCHEN AUSWERTUNG EINES GEGENSTANDSARRAYS

(57) Abstract

The invention relates to an array for optical evaluation of an object array, to which a microlens array (MLA), preferably an exchangeable and/or rotational microlens array, and a field lens with an illuminating device coupled by means of a beam splitter, preferably a rotational beam splitter, are pre–assigned in the direction of a detector array, wherein said illuminating device is coupled between the field lens and an objective.

(57) Zusammenfassung

Anordnung zur optischen Auswertung eines Gegenstandsarrays, dem in Richtung eines Detektorarrays ein vorzugsweise auswechselbares und/oder ausschwenkbares Mikrolinsenarray (MLA) sowie eine Feldlinse vorgeordnet ist, mit einer über einen vorzugsweise ausschwenkbaren Strahlteiler eingekoppelten Beleuchtung, wobei diese zwischen der Feldlinse und einem Objektiv eingekoppelt wird.

LEDIGLICH ZUR INFORMATION

Codes zur Identifizierung von PCT-Vertragsstaaten auf den Kopfbögen der Schriften, die internationale Anmeldungen gemäss dem PCT veröffentlichen.

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Titel:

Anordnung zur optischen Auswertung eines Gegenstandsarrays

Es zeigen:

Fig. 1: Den vollständigen Strahlengang, beispielsweise bei der Fluoreszenzmessung

Fig.2 : Den Strahlengang bei der Absorptionsmessung

Fig.3 : Den Strahlengang bei der Luminsetzenzmessung

Fig.4 : Den Strahlengang ohne MLA

Beschreibung des Strahlengangs

Der optische Aufbau des ist in drei wesenliche Bestandteile gegliedert.

1. Ein Minilinsen-Array (MLA) (2) zur Fokusierung von Licht in kleine Bereiche (Probvolumen) der mit Probensubstanz gefüllten Näpfe (1a-1d) einer Mikrotiterplatte (MTP) (1). Das MLA (2) dient auch dem Sammeln von aus dem Probvolumen emittiertem Licht im Falle von Fluoreszenz- oder Lumineszenz-Anwendungen.
2. Einer Teleskop-Anordnung der Linsen 3,11 und eines Kollimators (14) zur Beleuchtung des Minilinsenarrays 2. Als Lichtquelle kann der Ausgang eines Lichtleiter dienen, wie in der Zeichnung dargestellt die Lampe selbst..
3. Einer Feldlinse (3) und eines Objektivs (6) zur telezentrischen Abbildung der Pupillen des MLA (2) auf einen CCD-Array-Detektor (7).

Das Minilinsen-Array besteht aus einer regelmäßigen Anordnung kleiner Linsen oder Objektive. Vorzugsweise ist die Anordnung der Minilinsen ein rechtwinkeliges Raster. In jedem Fall ist die Anordnung der Minilinsen der Geometrie des Probenbehälter-Array bzw. der MTP angepaßt.

Die dem MLA (2) zugewandte Frontlinse (3) des Teleskops für die Beleuchtung dient gleichzeitig als Feldlinse der telezentrischen Abbildung der MLA-Pupillen.

1. Der Anregungs-Strahlengang

Das aus dem Lichtleiter (15) austretende Licht wird durch einen Kollimator (14) gesammelt. Der Kollimator (14) bildet zusammen mit der kleinen, kurzbrennweitigen Teleskoplinse (11) den Lichtleiterausgang auf die Zwischenbildebene (9) des Teleskops 3,11 ab. Die große, langbrennweitige Teleskoplinse (3) nimmt das Licht aus der Zwischenbildebene (9) auf und überführt es in ein Bündel geringer Divergenz, mit dem das MLA (2) von seiner probenabgewandten Seite her beleuchtet wird. Jede einzelne Linse (2a..2d) des MLA (2) fokussiert das Licht dann in einen ihr zugeordneten Napf (1a..1d) der Mikrotiterplatte (1).

Zwischen dem Kollimator (14) und der kleinen Teleskoplinse (11) befindet sich die Aperturblende (12) des Beleuchtungsteleskops und Abschwächungsfilter (13). Die Aperturblende (12) definiert die Form des Strahlquerschnitts und hält überflüssiges Licht aus dem Strahlengang fern. Das dient der Verminderung von Signalübersprechen und einer Verringerung des Streulichtuntergrundes im Nachweis-Strahlengang. Die Aperturblende (12) befindet sich in einer Ebene, die zur Ebene der Minilinsenpupillen konjugiert ist.. Die Aperturblende (12) bildet also verkleinert den äußeren Umriß des MLA (2) nach. Die Aperturblende kann zur besseren Streulichtunterdrückung auch als Lochblenden-Array ausgeführt werden.

In der Zwischenbildebene (9) befindet sich die Feldblende (9a) des Beleuchtungsteleskops. Die Zwischenbildebene (9) wird durch die große Teleskoplinse (3) und die Linsen (2a..2d) des MLA (2) in die Näpfe (1a..1d) der MTP (1) abgebildet. Die Feldblende (9a) definiert also den Bündelquerschnit des Lichtes innerhalb der Näpfe (1a..1d).

Der Anregungsfilter (10) dient dazu den Spektralbereich der Beleuchtung zu definieren.

Über den Spiegel (8) wird das von den Proben kommende Licht in den auch für die Detektion verwendeten Strahlengang eingespiegelt.
Durch die Anordnung des Spiegels 8 vor dem Objektiv 6 kann auf einfache Weise ein anderer Beleucghtungsmodus gewählt werden.
Wird das Gerät zur Floureszenz-Analyse eingesetzt, ist der Spiegel (8) als dichroitischer Strahlteiler ausgeführt. Der Spekrtralbereich des anregenden Lichts wird reflektiert, der zu detektierende Spektralbereich dagegen transmitiert. Dient das Gerät zur Detektion von Lumineszenz, kann die Einspiegelung durch Spiegel 8 und damit die Beleuchtung entfallen und der Strahlengang umfaßt nur noch den Nachweisstrahlengang, wie noch dargestellt wird.

2. Der Nachweis-Strahlengang

Das vom Probvolumen emittierte Licht wird durch die Minilinsen (2a..2d) kollimiert. Jedem Napf (1a..1d) der MTP (1) ist dabei eine Minilinse (2a..2d) zugeordnet. Das kollimierte Licht, das aus der Pupille der Minilinsen austritt, wird von der großen Teleskoplinse (3), die gleichzeitig als Feldlinse für die Pupillen-Abbildung dient, in die zur anregungsseitigen Zwischenbildebene (9) konjugierten Zwischenbildebene (4) fokusiert. In der Zwischenbildebene (4) sind also die Bilder der Probvolumina aus allen Näpfen (1a..1d) der MTP (1) überlagert. Die Blende (4a) definiert das beobachtete Probvolumen in jedem Napf. Vorzugsweise ist die Blende (4a) genauso groß wie die Feldblende (9a) der Beleuchtung.
Die Blende (4a) ist gleichzeitig die Aperturblende der Pupillenabbildung. Die Abbildung der Pupillen der Minilinsen (2a..2d) auf den CCD-Array-Detektor (7) erfolgt durch das Objektiv (6).

Der Emissionsfilter (5) dient dazu den nachgewiesenen Spektralbereich zu definieren.

Die Umlenkspiegel (16,17,18) dienen dazu den Strahlengang in eine kompakte Form zu bringen. Hierbei ist eine Mehrfachfaltung durch mehrere Spiegel dankbar.

Beschreibung der Meßmodi

Grundsätzlich lassen sich verschiedene Meßmethoden auf die in der MTP befindlichen Proben anwenden. Auf der Basis des oben beschriebenen Strahlengangs können die Messungen einer Methode in mehreren Näpfen parallel durchgeführt werden. Bisher sind folgende Meßmethoden in Betracht gezogen worden:

1. Absorption
2. Fluoreszenz
3. Lumineszenz
4. Zeitaufgelöste Fluoreszenz-Detektion
5. Polarisations abhängige Fluoreszenz (Absorption???)

Absorption

Bei Absorptionsmessungen kommt nur der Anregungsstrahlengang zur Anwendung.
Der Strahlteiler 8 kann gegen einen Vollspiegel ausgetauscht werden.
Die Detektion des durch die Probe transmitierten Lichts erfolgt durch ein Photodioden-Array (19), das so dicht als möglich den Probenbehältern nachgeordnet ist..
Durch den oben beschriebenen Strahlengang wird die probenabgewandte Seite des MLA homogen beleuchtet, so daß jeder Napf mit der gleichen Intensität durchstrahlt wird. Das MLA ist für Absorptionszwecke so auszulegen, daß die Begrenzungen der Näpfe die durch die Minilinsen geformten Strahlbündel nicht beschneiden und das jedes Strahlbündel vollständig auf die ihm zugeordnete Empfängerfläche (19a..19d) des Photodioden-Arrays fällt.
Das bedeutet , daß für bestimmte MTP oder Probenbehälter auswechselbare MLA und Feldblenden 9a vorgesehen sein können, die bezüglich der Brennweiten und Krümmungsradien optimiert sind.

Fluoreszenz

Bei Fluoreszenzmessungen erfolgt die Anregung in der gleichen Weise wie im Falle von Absorptionsmessungen. Der Spiegel (8) wird aber durch einen

dichroitischen Strahlteiler mit hoher Transmission für das von der Probe emittierte Licht ersetzt.

Die Auslegung des MLA orientiert sich an der möglichst selektiven Anregung und dem Nachweis aus einem kleinen Volumen innerhalb des Napfes, d.h. eine hinreichende chromatische Korrektur ist mit einer hohen numerischen Apertur (größer gleich 0.5) verbunden.

Lumineszenz

Da die Probe selbstleuchtend ist kommt nur der Nachweis-Strahlengang zur Anwendung

Der Strahlteiler 8 kann ausgeschwenkt werden.

Es besteht allgemein und auch bei der Absorptionsmessung die Möglichkeit das MLA wegzulassen und eine direkte Abbildung des MTP-Bodens auf den CCD-Array-Detektor zu erzeugen. In diesem Fall kann die gesamte Platte auf einmal ausgelesen werden unabhängig davon wieviele Näpfe sie enthält. Das bedeutet zwar leichte Verluste an Sensitivität, jedoch können auch bei einer großen Anzahl von Kanälen alle Kanäle gleichzeitig ausgelesen werden.

Zeitaufgelöste Fluoreszenz-Detektion

Bei der zeitaufgelösten Fluoreszenz kommt der gleiche Strahlengang zur Anwendung wie bei der Fluoreszenz.

Die Anregung erfolgt durch eine Lichtquelle, die in der Lage ist kurze Lichtpulse (ca. 1ns) zu erzeugen, d.h. beispielsweise eine geeignete Blitzlampe.

Der verwendete Detektor muß in der Lage sein nach einer Verzögerung in der Größenordnung der Dauer des Anregungspulses eine Messung mit einer Integrationszeit in der gleichen Größenordnung im Takt der Bleuchtung durchzuführen.

Hierzu ist eine Mikrochannelplateverstärkte Kamera geeignet.

Gemessen wird die nach der Verzögerungszeit verbleibende Fluoreszenzintensität.

Polarisationsabhängige Fluoreszenz

Voraussetzung ist eine polarisationserhaltende Optik. Gemessen wird die Fluoreszenzintensität mit der zum Anregungslicht orthogonalen Polarisationsrichtung.
Hierzu können vor den Filtern 5 und 10 vorzugsweise zueinander senkrecht polarisierte Polfilter vorgesehen sein.

Patentansprüche

1.

Anordnung zur optischen Auswertung eines Gegenstandsarrays, dem in Richtung eines Detetorarrays ein vorzugsweise auswechselbares und/ oder ausschwenkbares Mikrolinsenarray (MLA) sowie eine Feldlinse vorgeordnet ist, mit einer über einen vorzugsweise ausschwenkbaren Strahlteiler eingekoppelten Beleuchtung,
wobei diese zwischen der Feldlinse und einem Objektiv eingekoppelt wird.

2.

Anordnung nach Anspruch1,
wobei die Beleuchtung zwischen der Feldlinse und einer vor dem Objektiv angeordneten Blende eingkoppelt wird.

3.

Anordnung nach mindestens einem der vorangehenden Ansprüche,
wobei mittels der Feldlinse und dem Objektiv eine telezentrische Abbildung der Pupillenebene des MLA auf das Detektorarray erfolgt

4.

Anordnung nach mindestens einem der vorangehenden Ansprüche,
wobei mittels der Feldlinse und einer zweiten Linse eine teleskopische Anordnung zur Beleuchtung des MLA erzeugt wird

5.

Anordnung nach mindestens einem der vorangehenden Ansprüche,
wobei zwischen der Feldlinse und der Blende ein oder mehrere Umlenkelemente zur Faltung des Beleuchtungs und/ oder Detektionsstrahlenganges vorgesehen sind.

6.

Anordnung nach mindestens einem der vorangehenden Ansprüche,

wobei die das Gegenstandsarray vorzugsweise zur Fokuseinstellung mindestens vertikal zur Beleuchtungsachse verschiebbar ist

7.
Anordnung nach mindestens einem der vorangehenden Ansprüche,
wobei zur zeitaufgelösten Fluoreszenzmessung die Beleuchtung intermittierend unterbrochen wird und eine zum Beleuchtungstakt synchronisierte, vorzugsweise zeitversetzte Detektion erfolgt.

8.
Anordnung nach Anspruch 7, mit einer Beleuchtung über eine Blitzlampe

9.
Anordnung nach mindestens einem der vorangehenden Ansprüche,
wobei die MLA zur Beobachtung des vollständigen Gegenstandsarrays aus dem Strahlengang ausschwenkbar ist

10.
Anordnung nach mindestens einem der vorangehenden Ansprüche,
wobei die Beleuchtung zur Lumineszenzdetektion ausschaltbar und/ oder ihr Einkoppelelement ausschwenkbar ist

11.
Anordnung nach mindestens einem der vorangehenden Ansprüche,
wobei zur Absorrptionsmessung dem Gegenstandsarray in Beleuchtungsrichtung ein zweites Detektorarray nachgeordnet ist

12.
Anordnung nach mindestens einem der vorangehenden Ansprüche,
wobei zur Anpassung an unterschiedliche Meßaufgaben und/ oder unterschiedliche Gegenstandsarrays das MLA gegen weitere MLA austauschbar ist.

13.

Kombinationsgerät zur Erfassung der Fluoreszenz und oder der zeitaufgelösten Fuoreszenz und / oder der Luminsezenz und / oder der Absorption eines beleuchteten Gegenstandsarrays mit einem Mikrolinsenarray (MLA) sowie eine Feldlinse sowie einem Detektorarray,
mit einer über einen und einer über einen Strahlteiler eingeblendeten Beleuchtung,
insbesondere nach einem der vorangehenden Ansprüche,
wobei das MLA und/ oder das Detektorarray austauschbar und/ oder ausschwenkbar sind und/ oder der Strahlteiler ausschwenkbar ist und/ oder ein weiteres Detektorarray zur Absorptionsmessung vorgesehen ist und/ oder Mittel zur Fokuseinstellung auf das Gegenstandsarray vorgesehen sind.

14.

Verwendung einer Anordnung nach einem der vorangehenden Ansprüche als Reader für Mikrotiterplatten

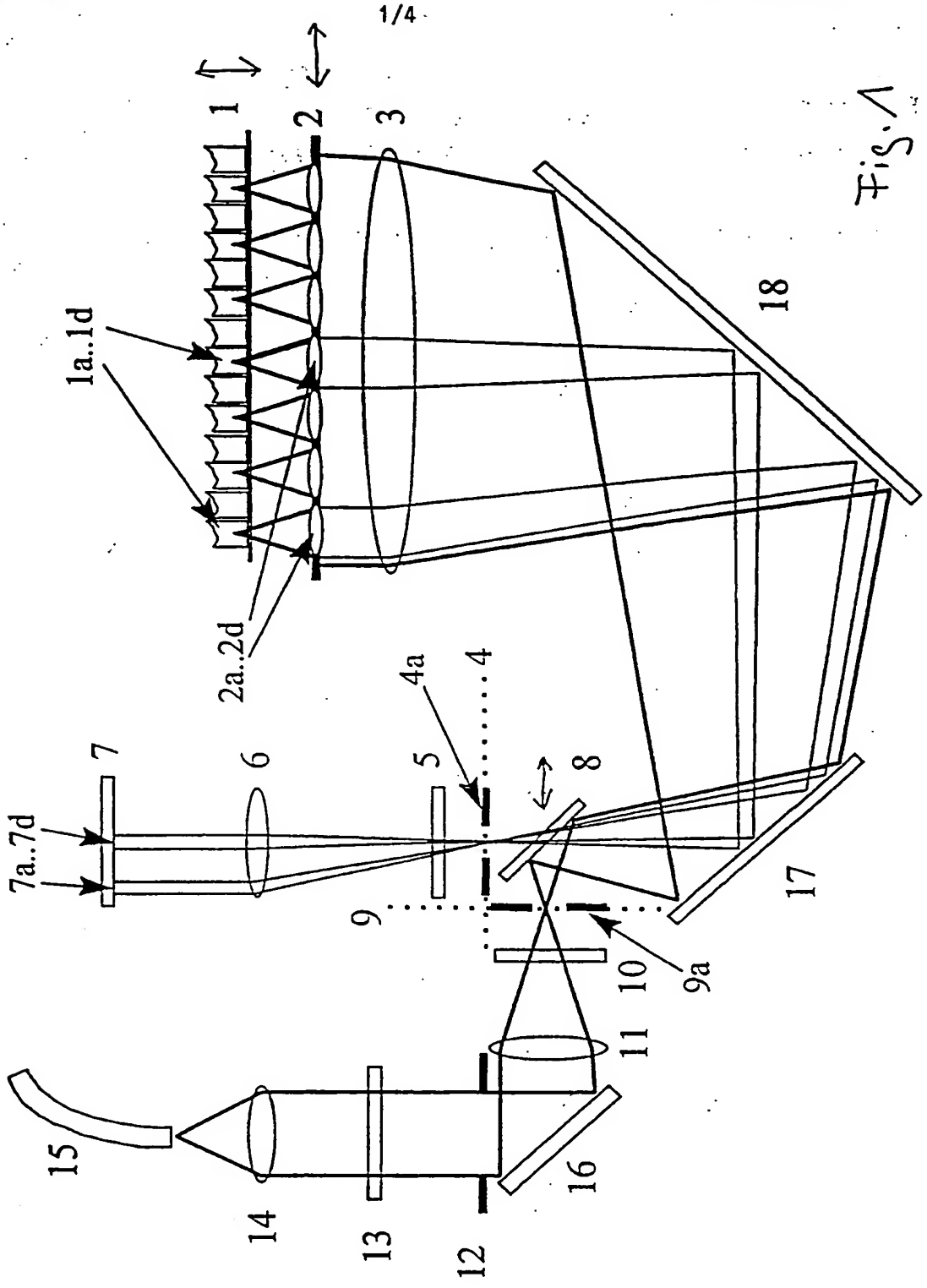


Fig. 1

Fluoreszenz-Reader

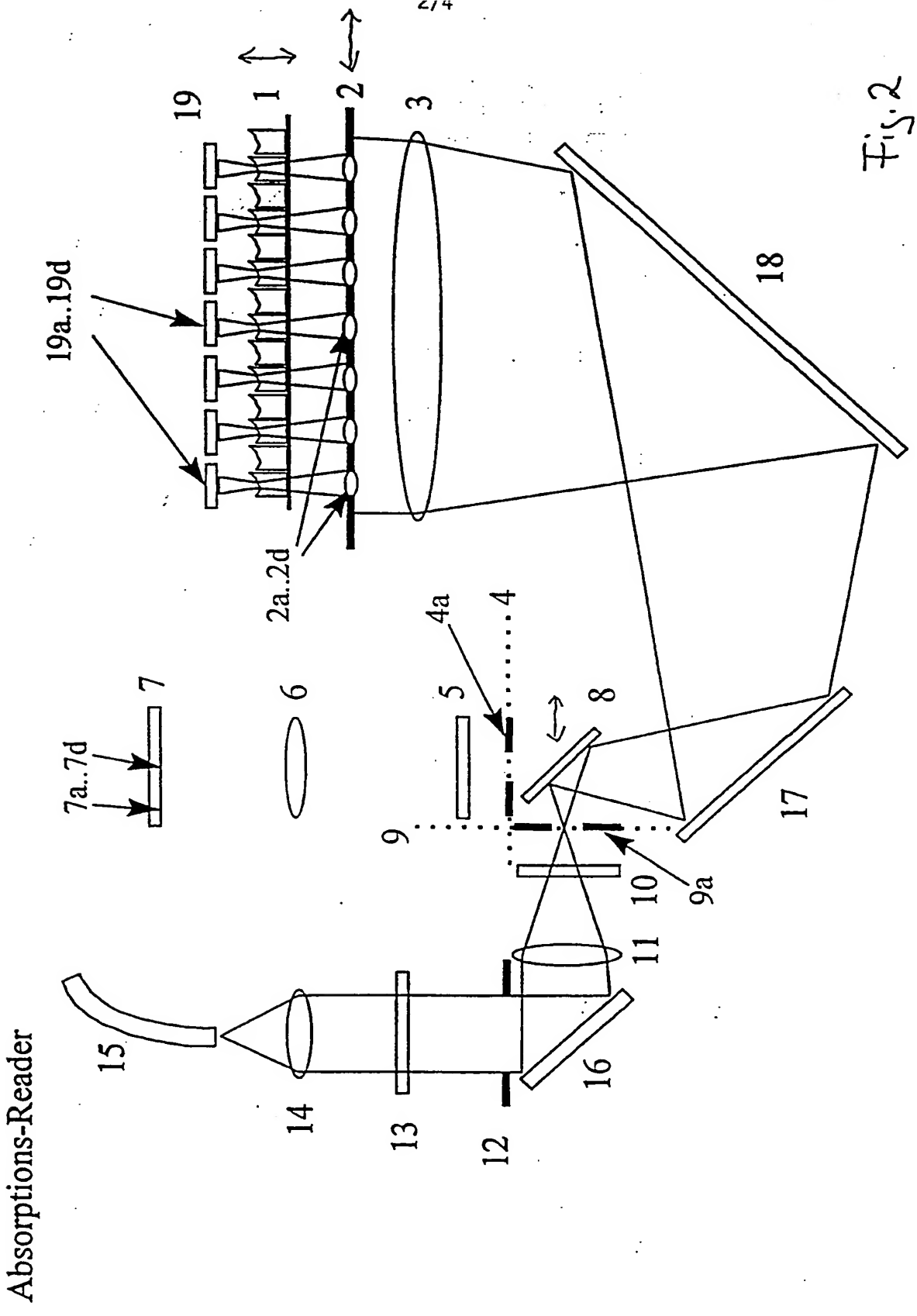

Absorptions-Reader
19a..19d
19
1
2
3
18
2a..2d
4a
4
5
6
7
7a..7d
8
9
9a
10
11
12
13
14
15
16
17

Fig. 2

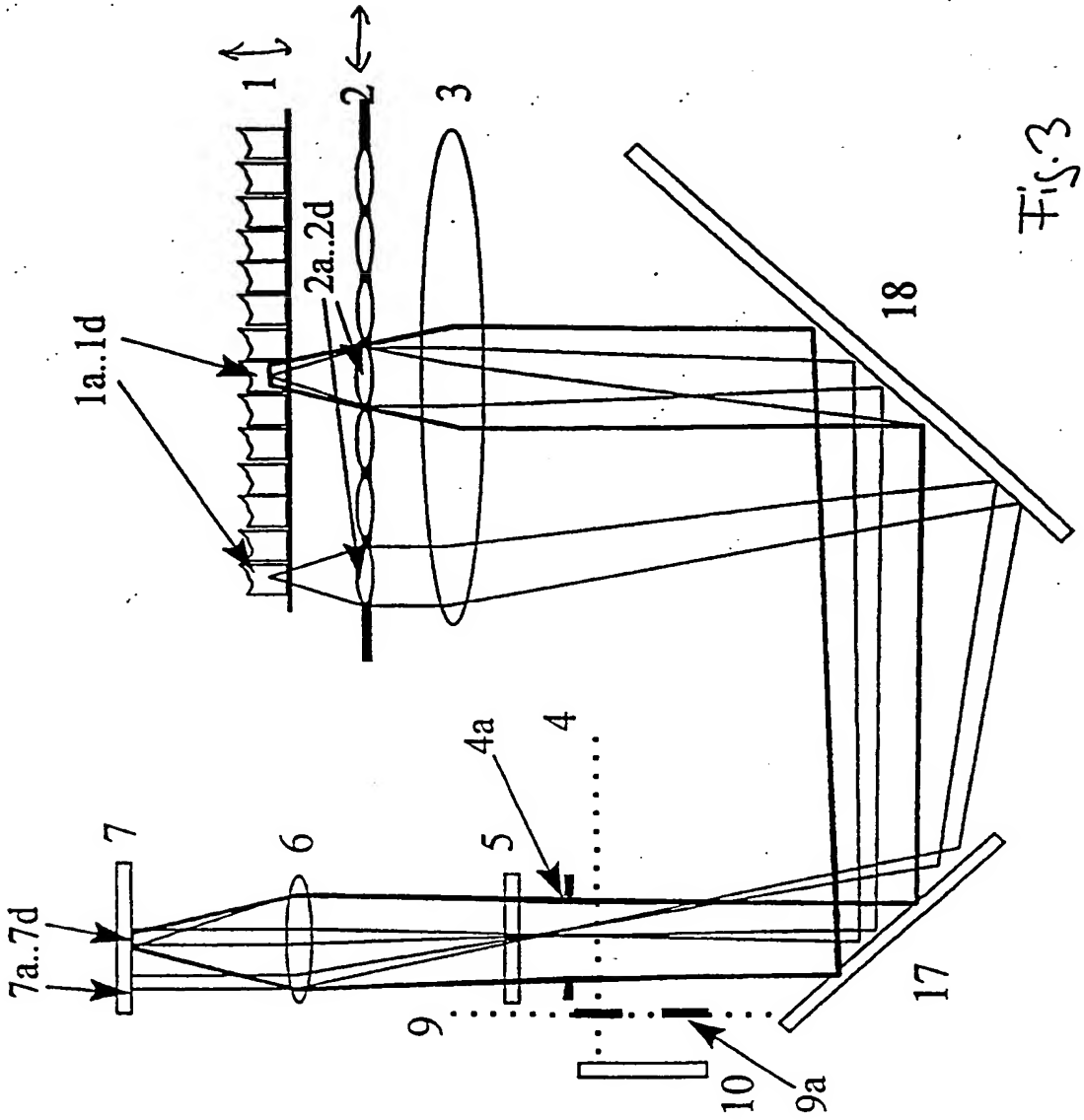
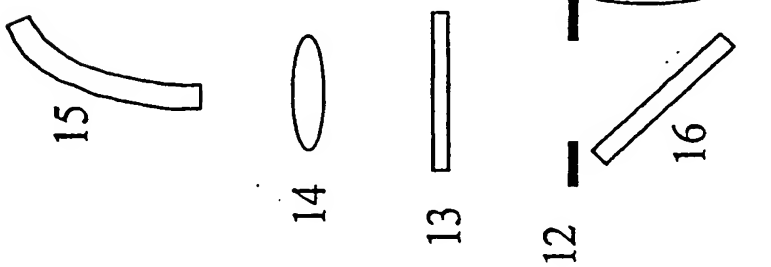


Fig.3

Lumineszenz-Reader



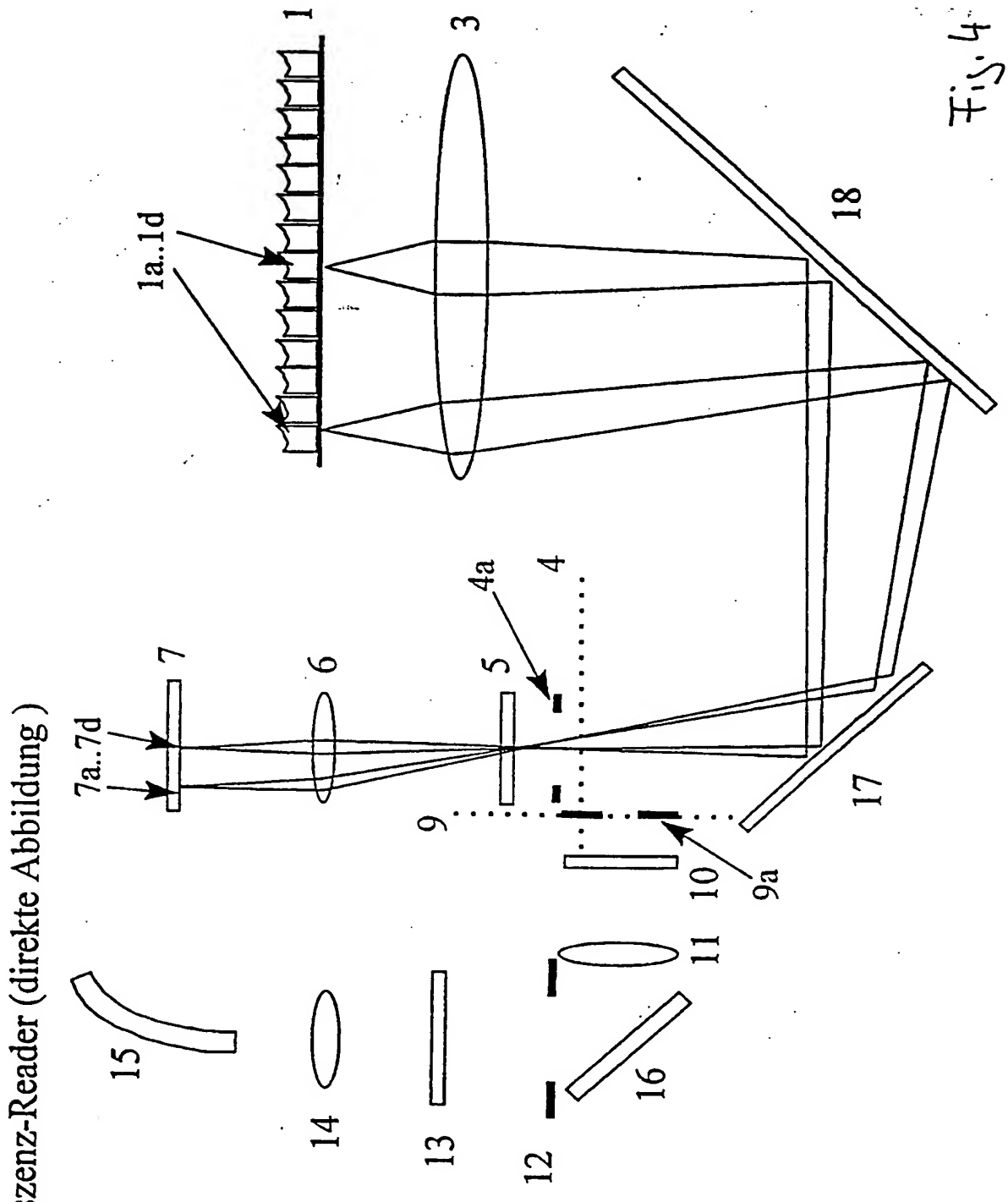

Lumineszenz-Reader (direkte Abbildung)
1
1a..1d
3
18
7
7a..7d
6
5
4a
4
9
10
9a
17
15
14
13
12
16
11

Fig. 4

(12) NACH DEM VERTRAG ÜBER DIE INTERNATIONALE ZUSAMMENARBEIT AUF DEM GEBIET DES PATENTWESENS (PCT) VERÖFFENTLICHTE INTERNATIONALE ANMELDUNG

(19) Weltorganisation für geistiges Eigentum
Internationales Büro

(43) Internationales Veröffentlichungsdatum
2. November 2000 (02.11.2000)

PCT

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WO 00/65325 A3

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13. April 2000 (13.04.2000)

(25) Einreichungssprache: Deutsch

(26) Veröffentlichungssprache: Deutsch

(30) Angaben zur Priorität:
199 19 092.5 27. April 1999 (27.04.1999) DE

(71) Anmelder *(für alle Bestimmungsstaaten mit Ausnahme von US)*: CARL ZEISS JENA GMBH [—/—]; Carl-Zeiss-Promenade 10, D-07745 Jena (DE).

(72) Erfinder; und

(75) Erfinder/Anmelder *(nur für US)*: SCHMIDT, Stefan [DE/DE]; Buchaer Str. 6 b, D-07745 Jena (DE).

(74) Gemeinsamer Vertreter: CARL ZEISS JENA GMBH; Carl-Zeiss-Promenade 10, D-07745 Jena (DE).

(81) Bestimmungsstaaten *(national)*: JP, US.

(84) Bestimmungsstaaten *(regional)*: europäisches Patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE).

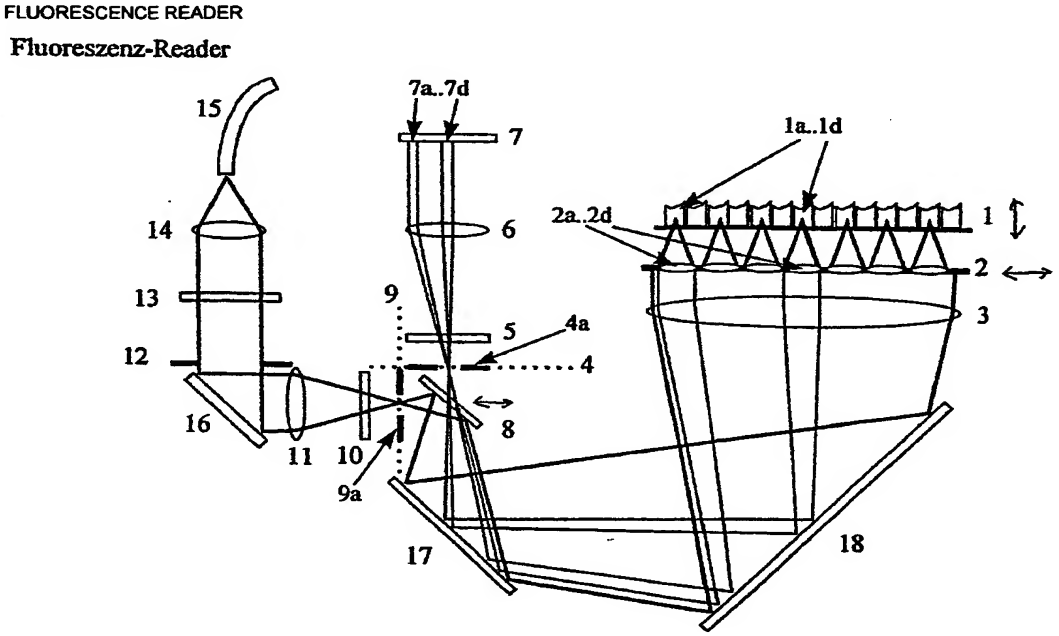
Veröffentlicht:
— *Mit internationalem Recherchenbericht.*

(88) Veröffentlichungsdatum des internationalen Recherchenberichts: 26. April 2001

[Fortsetzung auf der nächsten Seite]

(54) Title: ARRAY FOR OPTICAL EVALUATION OF AN OBJECT ARRAY

(54) Bezeichnung: ANORDNUNG ZUR OPTISCHEN AUSWERTUNG EINES GEGENSTANDSARRAYS



(57) Abstract: The invention relates to an array for optical evaluation of an object array, to which a microlens array (MLA), preferably an exchangeable and/or rotational microlens array, and a field lens with an illuminating device coupled by means of a beam splitter, preferably a rotational beam splitter, are pre-assigned in the direction of a detector array, wherein said illuminating device is coupled between the field lens and an objective.

[Fortsetzung auf der nächsten Seite]

WO 00/65325 A3

Zur Erklärung der Zweibuchstaben-Codes, und der anderen Abkürzungen wird auf die Erklärungen ("Guidance Notes on Codes and Abbreviations") am Anfang jeder regulären Ausgabe der PCT-Gazette verwiesen.

(57) Zusammenfassung: Anordnung zur optischen Auswertung eines Gegenstandsarrays, dem in Richtung eines Detektorarrays ein vorzugsweise auswechselbares und/oder ausschwenkbares Mikrolinsenarray (MLA) sowie eine Feldlinse vorgeordnet ist, mit einer über einen vorzugsweise ausschwenkbaren Strahlteiler eingekoppelten Beleuchtung, wobei diese zwischen der Feldlinse und einem Objektiv eingekoppelt wird.

INTERNATIONAL SEARCH REPORT

Inte. .onal Application No
PCT/EP 00/03306

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 G01N21/25

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 G01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, COMPENDEX, INSPEC

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 97 34171 A (JOHNSON KENNETH C) 18 September 1997 (1997-09-18) figures 1,18,19 --- -/--	1-14

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

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"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
27 July 2000	14/08/2000

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Mason, W

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INTERNATIONAL SEARCH REPORT

Inte ional Application No
PCT/EP 00/03306

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
X	BOGDANOV VALERY ET AL: "Parallel, confocal, and complete spectrum imager for fluorescent detection of high-density microarray" PROCEEDINGS OF THE 1999 THREE-DIMENSIONAL AND MULTIDIMENSIONAL MICROSCOPY: IMAGE ACQUISITION AND PROCESSING VI;SAN JOSE, CA, USA JAN 24-JAN 25 1999, vol. 3605, 1999, pages 298-307, XP000917120 Proc SPIE Int Soc Opt Eng;Proceedings of SPIE - The International Society for Optical Engineering 1999 Society of Photo-Optical Instrumentation Engineers, Bellingham, WA, USA page 299 -page 301; figure 1	1-14
A	US 4 892 409 A (SMITH HARRY F) 9 January 1990 (1990-01-09) figure 4B	1-14
A	DE 197 25 050 A (FRAUNHOFER GES FORSCHUNG ;INST PHYSIKALISCHE HOCHTECHNOL (DE)) 17 December 1998 (1998-12-17) figure 2	1-14
A	US 5 112 134 A (HUMPHRIES GILLIAN M ET AL) 12 May 1992 (1992-05-12) figure 1	1-14
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A	WO 98 30889 A (MEDISPECTRA INC) 16 July 1998 (1998-07-16) figures 3,4,4A	1-14
A	DE 196 24 421 A (ZEISS CARL FA) 2 January 1997 (1997-01-02) figure 1	1-14

INTERNATIONAL SEARCH REPORT

information on patent family members

Inter nal Application No
PCT/EP 00/03306

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INTERNATIONALER RECHERCHENBERICHT

Inte .onales Aktenzeichen
PCT/EP 00/03306

A. KLASSIFIZIERUNG DES ANMELDUNGSGEGENSTANDES
IPK 7 G01N21/25

Nach der Internationalen Patentklassifikation (IPK) oder nach der nationalen Klassifikation und der IPK

B. RECHERCHIERTE GEBIETE

Recherchierter Mindestprüfstoff (Klassifikationssystem und Klassifikationssymbole)
IPK 7 G01N

Recherchierte aber nicht zum Mindestprüfstoff gehörende Veröffentlichungen, soweit diese unter die recherchierten Gebiete fallen

Während der internationalen Recherche konsultierte elektronische Datenbank (Name der Datenbank und evtl. verwendete Suchbegriffe)
EPO-Internal, COMPENDEX, INSPEC

C. ALS WESENTLICH ANGESEHENE UNTERLAGEN

Kategorie°	Bezeichnung der Veröffentlichung, soweit erforderlich unter Angabe der in Betracht kommenden Teile	Betr. Anspruch Nr.
X	WO 97 34171 A (JOHNSON KENNETH C) 18. September 1997 (1997-09-18) Abbildungen 1,18,19 -/--	1-14

[X] Weitere Veröffentlichungen sind der Fortsetzung von Feld C zu entnehmen

[X] Siehe Anhang Patentfamilie

° Besondere Kategorien von angegebenen Veröffentlichungen :
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Datum des Abschlusses der internationalen Recherche	Absendedatum des internationalen Recherchenberichts
27. Juli 2000	14/08/2000

Name und Postanschrift der Internationalen Recherchenbehörde	Bevollmächtigter Bediensteter
Europäisches Patentamt, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31–70) 340–2040, Tx. 31 651 epo nl, Fax: (+31–70) 340–3016	Mason, W

1

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INTERNATIONALER RECHERCHENBERICHT

Int. Aktenzeichen
PCT/EP 00/03306

C.(Fortsetzung) ALS WESENTLICH ANGESEHENE UNTERLAGEN

Kategorie°	Bezeichnung der Veröffentlichung, soweit erforderlich unter Angabe der in Betracht kommenden Teile	Betr. Anspruch Nr.
X	BOGDANOV VALERY ET AL: "Parallel, confocal, and complete spectrum imager for fluorescent detection of high-density microarray" PROCEEDINGS OF THE 1999 THREE-DIMENSIONAL AND MULTIDIMENSIONAL MICROSCOPY: IMAGE ACQUISITION AND PROCESSING VI;SAN JOSE, CA, USA JAN 24-JAN 25 1999, Bd. 3605, 1999, Seiten 298-307, XP000917120 Proc SPIE Int Soc Opt Eng;Proceedings of SPIE - The International Society for Optical Engineering 1999 Society of Photo-Optical Instrumentation Engineers, Bellingham, WA, USA Seite 299 -Seite 301; Abbildung 1	1-14
A	US 4 892 409 A (SMITH HARRY F) 9. Januar 1990 (1990-01-09) Abbildung 4B	1-14
A	DE 197 25 050 A (FRAUNHOFER GES FORSCHUNG ;INST PHYSIKALISCHE HOCHTECHNOL (DE)) 17. Dezember 1998 (1998-12-17) Abbildung 2	1-14
A	US 5 112 134 A (HUMPHRIES GILLIAN M ET AL) 12. Mai 1992 (1992-05-12) Abbildung 1	1-14
A	WO 96 23213 A (MURRAY ANTHONY J ;STEGEMANN JOSEF (DE); ANSORGE WILHELM (DE)) 1. August 1996 (1996-08-01) Abbildungen 1,3A,3B	1-14
A	WO 98 30889 A (MEDISPECTRA INC) 16. Juli 1998 (1998-07-16) Abbildungen 3,4,4A	1-14
A	DE 196 24 421 A (ZEISS CARL FA) 2. Januar 1997 (1997-01-02) Abbildung 1	1-14

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Angaben zu Veröffentlichungen, die zur selben Patentfamilie gehören

Internationales Aktenzeichen
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DE 19624421	A	02-01-1997	KEINE		